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DERMATITIS VACCINICA

(KAPOSI'S VARICELLIFORM ERUPTION)

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The disease reported in this communication as dermatitis vaccinica has been called by many names, the best known perhaps being Kaposi's varicelliform eruption, pustulosis vacciniformis acuta (Freud) and eczema vaccinatum. The other synonyms include pustulosis acuta varioliformis (Juliusberg), postvaccinal eruption, *vaccine généralisée,* generalized vaccinia, vaccinoderma, *vaccinosi accidentale* (Venturi), eczema varicellatum (or variolatum) and eczema herpetiforme.

The relationship of dermatitis vaccinica to vaccinia virus is denied by many authors. Some believe it is due to staphylococci; others, that it is a herpetic eruption. This uncertainty is due to the fact that in many cases the inoculated cornea of the rabbit does not show the Guarnieri bodies, that a history of contact with a recently vaccinated person is not obtained or that in some cases a subsequent vaccination of the patient gives positive results.

However, the clinical course and the histologic structure of the pustule are decidedly different from known staphylococcic infections, from herpes simplex and from varicella. I believe that the disease is related to vaccinia virus, and I propose to call it dermatitis vaccinica. In my opinion dermatitis vaccinica and generalized vaccinia (so-called "true vaccinia") are varieties of the same disease.

Whatever the cause of dermatitis vaccinica may be, it is a clinical entity and a dermatologic and pediatric rarity. I have heard dermatologists and pediatricians of large experience say that they had never encountered a case. Little has been done to acquaint the members of the medical profession with it. The illustration of Kaposi's varicelliform eruption in the textbook of Sutton and Sutton greatly helped in the diagnosis. This is in sharp contrast with the lack of illustrations or even mention of postvaccinal eruptions in most treatises on dermatology, pediatrics and communicable diseases.

From the Skin Service of the Charles V. Chapin Hospital.

Read at the monthly meeting of the W. W. Keen Club, Nov. 14, 1941.

Postvaccinal eruptions in general are rare. According to Lynch,[1] Schamberg had observed 5 cases in fifteen years, Brayton 6 or 7 in 40,000 cases, and Chauveau 4 in 500,000 vaccinations, Hastud 4 in 40,000, Vogt 5 in 100,000 and Wolff none in 7,000. Dermatitis vaccinica has been extensively discussed by Ellis[2] and Tedder.[3] To avoid repetition I refer to these two outstanding papers for more details. Other valuable papers not cited by Ellis and Tedder are by Venturi,[4] Lynch,[1] McLachlan and Gillespie,[5] Graves and Dowman,[6] Albrigo,[7] King[8] and Höffken.[9]. Wollnitza's paper[10] is particularly interesting because of the demonstration of the virus of vaccinia in the urine and blood of the patient. The condition was called generalized vaccinia, but the involved areas were only the head and later the genitals. The child was treated with serum of a recently vaccinated person.

The main features of dermatitis vaccinica are: a preexisting acute or chronic dermatosis, usually infantile eczema, a susceptibility to the vaccinia virus, a contact with the virus, the consequent varioliform eruption and the following immunity to the virus of vaccinia.

REPORT OF CASES

CASE 1.—A 15 month old white boy, born in the United States of Italian extraction, had suffered from infantile eczema involving the arms, the upper part of the chest, the neck and part of the face for nine months. About Feb. 10, 1941 he began to have a high temperature and the eczematous areas became covered with blisters and bloody crusts. The axillary lymph nodes were considerably enlarged. He was admitted to the Charles V. Chapin Hospital with a diagnosis of impetigo superimposed on infantile eczema.

The face, scalp, neck, arms and upper parts of the chest and back were covered with a vesiculopustular rash. The rest of the skin was rough and dry. Enlarged lymph nodes were present in the occipital region, on the neck and in the armpits. Internal physical examination revealed nothing of importance.

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1. Lynch, F. W.: Dermatologic Conditions of the Fetus with Particular Reference to Variola and Vaccinia, Arch. Dermat. & Syph. **26**:997 (Dec.) 1932.
2. Ellis, F. A.: Eczema Vaccinatum: Its Relation to Generalized Vaccinia, J. A. M. A. **104**:1891 (May 25) 1935.
3. Tedder, J. W.: Eczema Vaccinatum, Arch. Dermat. & Syph. **34**:1008 (Dec.) 1936.
4. Venturi, T.: Sopra alcuni casi di vaccinosi accidentale, Dermosifilografo **3**:576, 1928.
5. McLachlan, A. D., and Gillespie, M.: Kaposi's Varicelliform Eruption: An Epidemic of Sixteen Cases, Brit. J. Dermat. **48**:337, 1936.
6. Graves, G. W., and Dowman, C.: Accidental Smallpox Vaccination and Eczema Vaccinatum, New York State J. Med. **37**:1833, 1937.
7. Albrigo, B.: Su un caso di infezione accidentale da vaccino, Dermosifilografo **13**:386, 1938.
8. King, A. D.: Kaposi's Varicelliform Eruption: A Report of Five Cases, in One of Which the Condition Began as Herpes Zoster, Arch. Dermat. & Syph. **39**:1035 (June) 1939.
9. Höffken, C. H.: Ein Beitrag zur Pustulosis vacciniformis acuta, Kinderärztl. Praxis **9**:3, 1938.
10. Wollnitza, E.: Beitrag zur Frage der Vaccina generalisata und Nachweis des Virus im Urin, Arch. f. Dermat. u. Syph. **177**:186, 1938.

His temperature rose to 102, 100 and 101 F. and then became normal. The urine was normal. A culture of material from the throat did not yield diphtheria bacilli. On February 14 the hemoglobin content was 94 per cent, the red blood cell count 4,200,000 and the white blood cell count 12,400, with 59 per cent polymorphonuclear leukocytes, 38 per cent lymphocytes, 1 per cent mononuclear leukocytes and 1 per cent basophils. The pustules yielded Staphylococcus aureus and hemolytic streptococci, the latter being predominant. On February 16 the hemoglobin content was 72 per cent, the red blood cell count 3,800,000 and the white blood cell count 11,800, with 56 per cent polymorphonuclear leukocytes, 36 per cent lymphocytes, 7 per cent mononuclear leukocytes and 1 per cent eosinophils.

Fig. 1 (case 1).—Distribution of the eruption.

On February 25 otitis media developed. The pus showed a pure culture of Staph. aureus.

Routine cutaneous tests with foods and pollens gave negative results. The therapy consisted of administration of sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) by mouth and in ointment form.

On March 5 he was sent home, but two weeks later his temperature rose to 104 F. and he returned to the hospital with impetigo. He was given sulfathiazole again by mouth and in ointment form, and his temperature dropped rapidly to normal. A blood culture gave negative results. A roentgenogram of the chest was normal. Greatly improved, he was sent home on March 23. Because of

a new relapse he returned to the hospital and then was discharged again, against medical advice, on April 9.

On July 26 he returned to the hospital for the fourth time, with a temperature of 105 F. and his area of eczema covered with what I thought was impetigo as severe as when first seen. The eruption started suddenly after the skin had been entirely clear for three weeks. The culture showed Staph. aureus, as before. However, the appearance of the lesions was no longer like that of impetigo contagiosa. The lesions consisted of firm, umbilicated, smallpox-like pustules, some isolated, some coalescent, distributed in the same areas, about the face, neck upper part of the chest and upper parts of the back and arms (fig. 1). The axillary lymph nodes were enlarged to the size of an orange.

A pustule was excised and a histologic examination by Dr. James T. Fallon showed the following picture. A section of skin and subcutaneous tissue showed a pustule involving the whole thickness of the epithelium and extending into the upper layers of the corium. The pustule was separated by a narrow strip of

Fig. 2 (case 1).—Low power magnification of a varioliform pustule.

practically normal epithelium in which the rete cones were greatly elongated, as were the cones at the lateral margins. The pustule was covered by thick layers of deeply acidophilic-staining necrotic epithelium which were narrowed at the periphery. It contained masses of cellular debris, polymorphonuclear leukocytes, large degenerated epithelial cells and portions of disintegrating hair follicles. The epithelial cells of the walls and bases were swollen and edematous; numbers of them contained mitotic figures. Separate disintegrated portions of epithelium were seen at the bases. The corium and subcutaneous tissues were infiltrated with lymphocytes, especially in the region surrounding the blood vessels and lymphatics. Thick, dense strands of fibrin were seen in the subcutis at the bases of the lesions. A number of small blood channels showed extensive degrees of angiitis with proliferation of their endothelial linings. The pathologic diagnosis was varioliform pustule (fig. 2).

The patient's temperature between July 26 and July 30 rose to 105 F. three times. The leukocytes numbered 23,600. He received sulfathiazole by mouth and locally in ointment form. Also, gentian violet and warm boric acid compresses were used.

The Paul test (inoculation of the content of a pustule into the cornea of the rabbit) was attempted, but the rabbit died soon after the inoculation for unknown reasons.

The parents were carefully questioned about the source of infection, about members of the family, friends or neighbors recently vaccinated, but the result of this investigation was negative.

The patient was sent home on August 11, against advice, but had to return to the hospital on August 13, for the fifth time, for the opening of a huge lymph node in his left axilla. When he was ready to go home, laryngeal diphtheria developed on September 15, for which he was intubated and received 40,000 units of diphtheria antitoxin. Later bronchopneumonia developed. He was discharged in good condition, except for enlarged tonsils, on October 22.

The areas involved by the pustular eruption healed without scars. Up to the time of writing he has been well with the exception of having dry and slightly scaly skin in the original areas of infantile eczema.

The child had gone through so much hardship that I thought it was advisable not to take the risk of an experimental vaccination to demonstrate his eventual immunity.

Case 2.—A 22 month old white boy, born in the United States of Italian extraction, had eczema on both arms, elbows and face since the age of 1 month. He was in good health otherwise.

On Oct. 6, 1941 he was brought to my office with a temperature of 103 F. and an eruption of three days' duration consisting of red macules becoming gradually vesicular and pustular. The lesions were firm and umbilicated, exactly as in the previously described case. He also suffered from diarrhea and coryza.

He was admitted to the Charles V. Chapin Hospital on October 7. He lay in bed crying, but not in acute distress. He was rational and cooperative. The physical examination revealed nothing abnormal. The temperature from October 7 to October 9 was between 105 and 101 F.; then it went down to normal.

He had received no vaccination or injections. There was a definite history of contact with two sisters, 6 and 5 years old respectively, who had been vaccinated three weeks previously. The mother recalled distinctly that the patient struck one sister over the vaccination area four days after the vaccination had been administered.

Cultures of material from the throat were negative for diphtheria. Culture of material from the pustules showed Staph. aureus, causing slight hemolysis, and a few colonies of hemolytic streptococci.

The administration of sulfathiazole in ointment form and by mouth was started the third day in the hospital. On the fifth day the temperature went down to normal. On the twelfth day use of sulfathiazole ointment was omitted and only boric acid ointment used. On the fourteenth day the oral administration of sulfathiazole was stopped. The total amount administered was 222.85 grains (14.48 Gm.).

After discharge the patient was vaccinated three times in succession, with negative results. The Paul test was not made. At present, with the exception of dryness and some itching of his eczematous areas, he is in good health. The eruption healed without scars.

COMMENT

If a history of exposure to vaccinia virus is important evidence in favor of a diagnosis of dermatitis vaccinica, the absence of this element cannot be held absolutely against it. In the case reported by Tedder,[3]

for example, a history of such exposure was not obtained until the parents of the patient had been repeatedly and carefully questioned. Tedder [3] cited a case from the literature in which contact took place in a bath tub in which a recently vaccinated child had bathed a short time previously and another case in which the affected child was left under the care of a woman whose child had been recently vaccinated.

A negative result of the inoculation of the cornea of the rabbit or a positive vaccination after recovery, of course, is a strong argument against a relation of dermatitis vaccinica to vaccinia virus. But I am inclined to give more importance to the clinical appearance, the clinical course and the histologic structure of the pustule. Staphylococci are found in all pyodermas, but dermatitis vaccinica has no clinical similarity to other pyodermas. Something must be accompanying the staphylococci. This something may reasonably be the virus of vaccinia.

Ellis [2] and Tedder [3] expressed the belief that eczema vaccinatum and vaccinia are the same thing. I do not see any reason to call the generalized (hematogenous) eruption vaccinia or "true vaccinia" and the localized (by external contact) eczema vaccinatum. They are vaccinal eruptions, one generalized and the other localized.

Tedder [3] stated that generalized vaccinia develops in a healthy skin while localized vaccinia develops in a damaged one. "Healthy skin" is a loose expression useful in popular talk. When one is confronted with a case of generalized vaccinia how can it be proved that the patient had a "healthy" skin?

Seidenberg [11] vaccinated the corneas of rabbits with the content of pustules of vaccinia, then with the content of vesicles of herpes simplex and then again with the content of pustules of vaccinia. The result was that the rabbits were immune against a reinfection with herpes simplex virus but showed no immunity against a reinfection with vaccinia virus. He concluded from this experiment that dermatitis vaccinica is not related to vaccinia but is a kind of herpetic eruption. However, he admitted that the presence of herpes virus in dermatitis vaccinica may be purely coincidental, and the experiment was done on only 3 rabbits.

The idea that dermatitis vaccinica could be a herpetic eruption has been expressed by others. But why is dermatitis vaccinica so rare and herpes simplex so common? Why does dermatitis vaccinica not recur, whereas recurrence is a characteristic of herpes simplex? Does impetigo or herpes simplex show such severity, such high temperature, such frquency of fatal outcome as reported for dermatitis vaccinica?

If dermatitis vaccinica is due to staphylococci (a pyoderma imitating the pyoderma of vaccinia [Höffken [9]] or streptococci, why should

11. Seidenberg, S.: Zur Aetiologie der Pustulosis vacciniformis acuta, Schweiz. Ztschr. f. allg. Path. u. Bakt. **4**:398, 1941.

it develop with firm, umbilicated varioliform pustules and not with the soft watery vesicles of the well known common impetigo? Why in some cases is there no vesicular stage preceding the pustular one (Bettley [12])? Why are infantile eczema and staphylococcic pyoderma so common and dermatitis vaccinica so rare? The firm, umbilicated pustules of dermatitis vaccinica are entirely different clinically (fig. 1) and pathologically (fig. 2) from the watery vesicles of varicella, herpes simplex or impetigo, and the clinical appearance and course should have their share in the diagnostic interpretation of a case. The immunity to three successive vaccinations in my second case is in favor of a relation of dermatitis vaccinica to the virus of vaccinia.

In regard to terminology, accidental vaccinosis and vaccinoderma are good terms. To eczema vaccinatum and the many other titles I prefer dermatitis vaccinica because, while eczema usually opens the door to the virus, any other dermatosis may do the same (erythema multiforme, impetigo, epidermolysis bullosa, hydroa, secondary syphilis, etc.). Any acute or chronic dermatosis may become "vaccinata" or "vaccinatum."

SUMMARY AND CONCLUSIONS

Two cases of dermatitis vaccinica are herein reported.

In 1 case a definite history of contact with two recently vaccinated sisters and immunity to repeated vaccinations after recovery favor a relation of dermatitis vaccinica to vaccinia virus.

In both cases, as in others reported in the literature, the clinical features and course are much different from those of herpes simplex, varicella, impetigo and other pyodermas, so that a relation of dermatitis vaccinica, for example, to herpes simplex is most unlikely.

Both patients recovered with no scars.

The term dermatitis vaccinica is suggested as preferable for either the generalized or localized eruption, which are considered variations of the same process.

Dermatitis vaccinica is a pediatric and dermatologic rarity.

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12. Bettley, F. R.: Kaposi's Varicelliform Eruption: Some Experimental Findings, Brit. J. Dermat. **52**:222, 1940.

ACTION OF SULFONAMIDE COMPOUNDS ON BLASTOMYCES DERMATITIDIS IN VITRO

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An attempt has been made to test in vitro the efficacy of several drugs of the sulfonamide series against Blastomyces dermatitidis. The drugs used included sulfanilamide, sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine), sodium sulfapyridine, sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole), sodium sulfathiazole, sulfadiazine (2-[paraaminobenzenesulfonamido]-pyrimidine) and sulfaguanidine (sulfanilylguanidine). It is known that blastomycosis (Gilchrist's disease) can be treated effectively when involvement is limited to the cutaneous form [1] through the use of desensitization of the patient to the organism followed by administration of potassium iodide and roentgen therapy. Systemic blastomycosis, on the other hand, is not as responsive therapeutically.[2] It is this fact which prompted the present experiments.

MATERIALS AND METHODS

Satisfactory experimental use of the sulfonamide compounds is limited to some extent by the fact that some are only slightly soluble.[3]

From the Section of Dermatology and Syphilology of the Department of Medicine, Duke University School of Medicine.

1. (*a*) Martin, D. S., and Smith, D. T.: Blastomycosis (American Blastomycosis, Gilchrist's Disease): Report of Thirteen New Cases, Am. Rev. Tuberc. **39**:488 (April) 1939. (*b*) Hemphill, J. E., and Noojin, R. O.: North American Cutaneous Blastomycosis Treated with Superficial Roentgen Therapy: A Report of Four Cases, Am. J. Roentgenol. **48**:643 (Nov.) 1942. (*c*) Callaway, J. L., and Moseley, V.: Primary Cutaneous Gilchrist's Disease, South. M. J. **33**:622 (June) 1940.

2. Martin, D. S., and Smith, D. T.: Blastomycosis (American Blastomycosis, Gilchrist's Disease): Review of Literature, Am. Rev. Tuberc. **39**:275 (March) 1939. Callaway and Mosely.[1c]

3. (*a*) Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1941. (*b*) Marshall, E. K., Jr.; Bratton, A. C.; White, H. J., and Litchfield, J. T., Jr.: Sulfanilylguanidine: A Chemotherapeutic Agent for Intestinal Infections, Bull. Johns Hopkins Hosp. **67**:163 (Sept.) 1940. (*c*) Feinstone, W. H.; Williams, R. D.; Falff, R. T.; Huntington, E., and Crossley, M. L.: The Toxicity, Absorption, and Chemotherapeutic Activity of 2-Sulfanilamidopyrimidine (Sulfadiazine), ibid. **67**:427 (Dec.) 1940.

Clinically they should be effective with concentrations in the blood of 10 mg. per hundred cubic centimeters or less, since higher concentrations not only may be difficult to maintain but may carry definite risks due to increased frequency of drug intoxication.[4] Therefore, if blood levels of 10 mg. per hundred cubic centimeters are ineffective, oral use of the medicament probably is of little or no value. Thus, the solubility of the sulfonamide compounds and their limited concentrations in the blood were of considerable importance in determining a suitable approach regarding the effectiveness of these compounds against B. dermatitidis. Two methods of approach were found to be satisfactory.

Experiment 1.—A suspension in sterile physiologic solution of sodium chloride, 1:50 by volume, was made of the yeastlike form of B. dermatitidis grown on Sabouraud's dextrose agar at 37 C. for one week. Buffered beef infusion broth with a p_H of 7.4 was used as the testing medium with the sulfonamide compounds so that the following concentrations (per hundred cubic centimeters) might be obtained: sulfanilamide, 20 mg.; sodium sulfapyridine, 20 mg.; sodium sulfathiazole, 20 mg.; sulfapyridine, 10 mg.; sulfathiazole, 10 mg.; sulfadiazine, 10 mg., and sulfaguanidine, 10 mg. Each solution was sterilized by filtration through a Seitz filter pad, and the solutions were tested for sterility and for the definite concentration of each particular sulfonamide drug by chemical determinations.[5] To each of fifteen sterile test tubes was added 9 cc. of beef infusion broth containing 20 mg. of sulfanilamide per hundred cubic centimeters. These tubes were inoculated with 1 cc. of a 1:50 saline suspension of live virulent B. dermatitidis and were designated group A. At the same time, to serve as a control, fifteen additional sterile test tubes containing 9 cc. of beef infusion broth were inoculated with 1 cc. of a 1:50 saline suspension of the same organisms and designated as group B. The thirty tubes were incubated at 37 C. After five, ten and twenty days' incubation five tubes each from groups A and B were removed from the incubator and 1 cc. of the mixture in each of the tubes was pipetted into sterile Petri dishes. To each Petri dish was added 20 cc. of molten Sabouraud's dextrose agar, and each dish was rotated to insure adequate distribution of the organisms throughout the medium. The Petri dishes were incubated at 37 C. for twenty-one days. At the end of this period the growth of organisms was recorded. In an identical manner sulfapyridine, sodium sulfapyridine, sulfathiazole, sodium sulfathiazole, sulfadiazine and sulfaguanidine were tested.

Experiment 2.—Two hundred cubic centimeters of Sabouraud's dextrose agar was divided equally into two flasks. To one flask 125 mg. of sulfanilamide was added, making a concentration of 125 mg. per hundred cubic centimeters. The two flasks were placed in a boiling water bath for thirty minutes, being constantly rotated to insure adequate distribution of the drug throughout the medium. Twenty cubic centimeter portions were added to sterile Petri dishes. This resulted in five Petri dishes containing Sabouraud's medium, which served

4. Marshall, E. K., Jr.; Bratton, A. C.; Edwards, L. B., and Walker, E.: Sulfanilylguanidine in the Treatment of Acute Bacillary Dysentery in Children, Bull. Johns Hopkins Hosp. **68**:94 (Jan.) 1941. Footnotes 3 *a* and *c*.

5. The concentrations of the sulfonamide compounds were checked by the Duke Biochemistry Laboratory by the identical method with which levels of these compounds in the blood are determined.

as a control, and five Petri dishes containing Sabouraud's medium plus sulfanilamide in a concentration of 125 mg. per hundred cubic centimeters.

The plates were incubated at 37 C. for twenty-four hours to test for sterility. Each plate was streaked with a loopful of a heavy saline suspension of a pure culture of the yeastlike form of B. dermatitidis. All plates were incubated at 37 C. for at least twenty-one days. In an identical manner the remaining six sulfonamide drugs were tested in concentrations of 125 mg. per hundred cubic centimeters. After this all seven drugs were tested in the following concentrations: 50, 75, 150, 175, 200 and 250 mg. per hundred cubic centimeters.

TABLE 1 (Experiment 1).—*Effect of Sulfonamide Compounds on Growth of Blastomyces Dermatitidis*

	Concentration of Drug per 100 Cc.	Incubation Period (With Drug)		
		5 Days	10 Days	20 Days
Control	.....	++++*	++++	++++
Sulfanilamide	20 mg.	++++	++++	++++
Sodium sulfapyridine	20 mg.	++++	++++	++++
Sodium sulfathiazole	20 mg.	++++	++++	++++
Sulfapyridine	10 mg.	++++	++++	++++
Sulfathiazole	10 mg.	++++	++++	++++
Sulfadiazine	10 mg.	++++	++++	++++
Sulfaguanidine	10 mg.	++++	++++	++++

* ++++ indicates luxuriant growth; 0, no growth.

TABLE 2 (Experiment 2).—*Effect of Sulfonamide Compounds in Varying Concentrations on Growth of Blastomyces Dermatitidis*

	Concentration						
Drug	50 Mg. per 100 Cc.	75 Mg. per 100 Cc.	125 Mg. per 100 Cc.	150 Mg. per 100 Cc.	175 Mg. per 100 Cc.	200 Mg. per 100 Cc.	250 Mg. per 100 Cc.
Sulfadiazine	±*	±	0†	0	0	0	0
Sulfanilamide	+‡	+	+	±	0	0	0
Sulfapyridine	+	+	+	+	±	±	0
Sodium sulfapyridine	+	+	+	+	+	+	0
Sulfathiazole	+	+	+	+	+	+	+
Sodium sulfathiazole	+	+	+	+	+	+	+
Sulfaguanidine	+	+	+	+	+	+	+

* ± indicates slightly diminished growth.
† 0 indicates greatly diminished or no growth.
‡ + indicates luxuriant growth.

RESULTS

Experiment 1.—When concentrations were used as listed in table 1, the fungus grew just as luxuriantly in mediums plus the sulfonamide compounds as it did in mediums without them. Table 1 also demonstrates that luxuriant growth occurred even when the fungus was exposed to the various compounds as long as ten to twenty days (figs. 1 and 2).

Experiment 2.—As demonstrated in table 2, in a concentration of 50 mg. per hundred cubic centimeters only sulfadiazine showed a partial inhibition of growth of B. dermatitidis. Also, in a concentration of 75 mg. per hundred cubic centimeters sulfadiazine showed partial inhi-

Fig. 1.—Blastomyces cultured in liquid medium twenty days and then incubated twenty-one days at 37 C. in Sabouraud's medium.

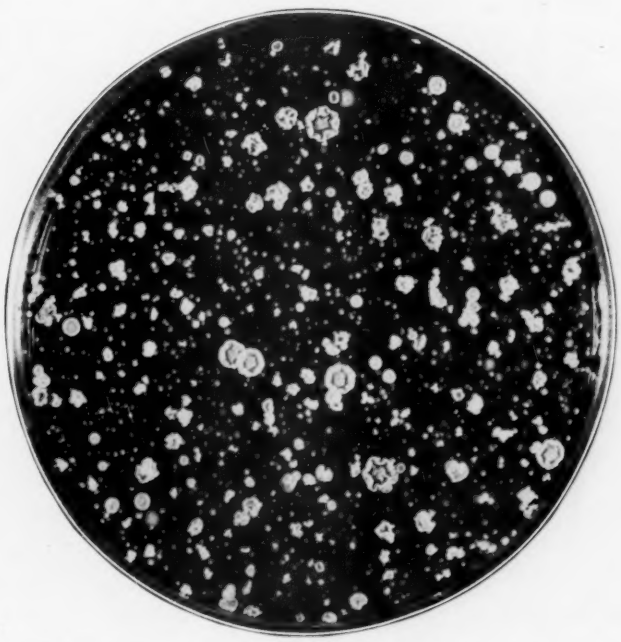

Fig. 2.—Blastomyces grown identically as explained in legend for figure 1 except that the liquid medium contained 20 mg. of sulfanilamide per hundred cubic centimeters.

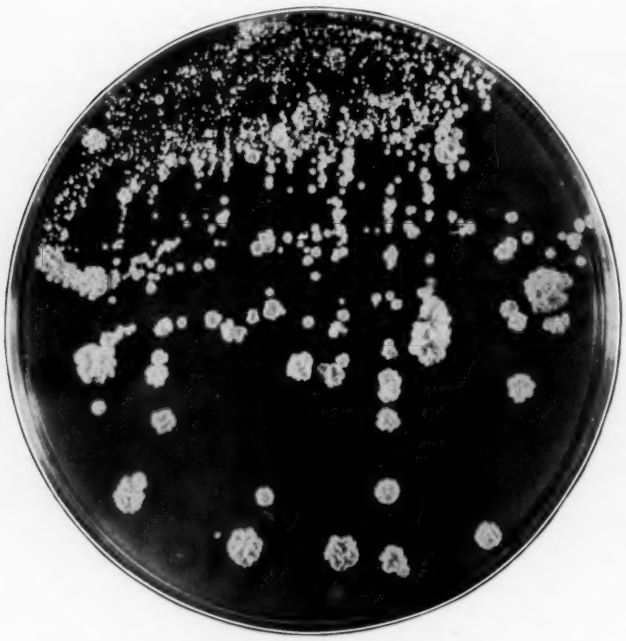

Fig. 3.—Blastomyces streaked on a Sabouraud plate.

Fig. 4.—Blastomyces streaked on a Sabouraud plate as in figure 3 except that Sabouraud's medium contained 175 mg. of sulfanilamide per hundred cubic centimeters. Complete inhibition of growth followed.

bition of growth of the fungus; in a concentration of 125 mg. sulfadiazine showed a decided inhibition of growth. None of the other drugs tested with this concentration showed any effect. The fungus cultured on medium containing sulfadiazine in a concentration of 150 mg. did not grow; with sulfanilamide its growth was partially inhibited, whereas growth was unaffected by the five other drugs tested. A concentration of sulfanilamide of 175 mg. per hundred cubic centimeters produced decided fungistatic effect (figs. 3 and 4). Sulfapyridine was found to inhibit growth partially in concentrations of 175 and 200 mg. and to inhibit growth completely only when a concentration of 250 mg. was reached. Sulfaguanidine, sulfathiazole and sodium sulfathiazole had no effect on the growth of the fungus even with a concentration of 250 mg. It is realized that the sodium salts of sulfapyridine and sulfathiazole were added to Sabouraud's dextrose agar, which is acid and contains no buffer. Up to a concentration of 250 mg., however, neither sulfathiazole nor sodium sulfathiazole was effective. On the other hand, sulfapyridine showed a slight effect at lower concentrations than did sodium sulfapyridine, and this may have been influenced both by a change in the sodium salt and by the change in p_H produced by the salt itself.

SUMMARY

In vitro experiments were carried out with sulfanilamide, sulfapyridine, sodium sulfapyridine, sulfathiazole, sodium sulfathiazole, sulfadiazine and sulfaguanidine to determine their effect on the growth of Blastomyces dermatitidis.

None of the drugs used were effective at levels as high as 10 mg. per hundred cubic centimeters, which is as high a blood level as is easily and safely maintained for any considerable time.

With higher concentrations sulfadiazine proved to be more effective than sulfanilamide, and both proved more effective than sulfapyridine, sodium sulfapyridine, sulfathiazole, sodium sulfathiazole and sulfaguanidine.

Decided fungistatic concentrations were not obtained with sulfadiazine, sulfanilamide, sulfapyridine and sodium sulfapyridine until high concentrations were reached. Sulfadiazine, which was the most efficient drug used, was not decidedly fungistatic until a concentration of 125 mg. per hundred cubic centimeters was used. Even with concentrations as high as 250 mg. per hundred cubic centimeters, sulfaguanidine, sulfathiazole and sodium sulfathiazole were ineffective.

CONCLUSIONS

The clinical applications suggested by these experiments would seem to indicate that the sulfonamide compounds would be ineffective if used orally or parenterally in treatment of blastomycosis, since the

concentrations required in vitro for inhibition of growth of Blastomyces dermatitidis are well above the clinical maximum tolerated drug levels. As a wet dressing or powder applied locally on cutaneous blastomycosis, sulfadiazine, sulfanilamide, sulfapyridine and sodium sulfapyridine, in the order named, might be effective therapeutically since the local concentration of the drugs would be considerably higher than that maintainable in the blood. We believe that sulfadiazine and sulfanilamide may be worth consideration for topical therapy of cutaneous blastomycosis.

Dr. Norman F. Conant and Miss Mary Poston gave helpful suggestions. Miss Louise Walker, Miss Dorothy Howard and Miss Doris Coltrane gave technical assistance.

Duke Hospital.

SUPERFICIAL PAPULONECROTIC TUBERCULID IN THE NEGRO

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For more than a quarter of a century the incidence of active tuberculous disease in the Negro has been on the upgrade.[1] The Negro's lack of resistance to the tubercle bacillus is well known, and it is not surprising to find hematogenous dissemination much more frequently in this race.[1] Tuberculids are common in the Negro, and in my experience, twenty-three years at the Harlem Hospital, the papulonecrotic variety was noted more often than any other type.

CLINICAL MANIFESTATIONS

The superficial nature and the inclination toward diminutive lesions are characteristic of the eruption in the Negro. This type of lesion occurs independent of the nodular variety, but it is not unusual to see the two types occur coincidentally. Papulonecrotic tuberculid is not an entirely benign disease. While active tuberculous foci often remain obscure and complicating disease of other viscera is uncommon, still the incidence of tuberculous disease of vital organs is greater in Negro than in white patients.

The eruption is nonpruritic and essentially superficial, and it is either localized or generalized with asymmetric tendencies. Exclusive of the scalp, lesions are seen everywhere on the cutaneous surface, but they are most commonly noted on the extensor aspects of both upper and lower extremities and on the buttocks. They are round and have convex surfaces which may show umbilication. The lesions are flesh colored, pinkish or reddish. There is either no areola or one with a tint similar to that of the lesions, and it is of variable width. Papules of different hues are encountered frequently in the same locality.

The lesions vary in size from that of a pinpoint to that of a pinhead and sometimes that of two or three pinheads, and on rare occasions they approach the size of a split pea. Surmounting them in a central or eccentric position it is customary to find brownish black superficial dotlike discolorations which assume, at rare intervals, a linear configuration; a single lesion does not contain more than one. These

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1. Pinner, M., and Kasper, J. A.: Pathological Peculiarities in the American Negro, Am. Rev. Tuberc. **26**:463 (Nov.) 1932.

pigmentary spots represent intraepidermal vesicles or pustules which develop early, and their forceful removal leaves tiny excavations. In 1 patient the vesicular element was decidedly pronounced and simulated varicella.

Fig. 1.—Involvement of the flexor aspects of the forearms. Lesions may be seen on the right palm. Note the large scar on the upper third of the right forearm. This resulted from an intracutaneous injection of 0.1 cc. of old tuberculin in a dilution of 1 to 10,000.

These epidermal discolorations have a close resemblance to comedos, and the eruption is readily mistaken for acne vulgaris, particularly if the lesions are sparse and are prevalent on the face, chest and back. In the absence of clinical epidermal necrosis the similarity to a sec-

ondary syphilid is considerable. Papular urticaria, iododerma and bromoderma may also be simulated.

Resolution occurs within one to five weeks. During this process the lesion may assume a lichenoid appearance. The minute central or eccentric epidermal vesicular or pustular area rises above the flattened surface as a rough crust which may have a whitish peripheral scale. When these pigmented crusts are especially prominent on the extensor aspects of the extremities, keratosis pilaris is simulated. After

Fig. 2.—Note the sparsity and asymmetric distribution of lesions.

complete resolution, smooth pinkish scars with hyperpigmented areolas are usually noted. Some scars contain additional minute shallow depressions, which appear at the sites of the antecedent epidermal necroses. The size of the cicatrix approximates that of the original lesion or that of the preceding epidermal discoloration. On occasion the scar is either flesh colored or entirely hyperpigmented.

Papulonecrotic tuberculids are noted on oral mucosa, female genitalia and nail beds. The asymptomatic buccal and palatal lesion is equivalent in every respect to that on the skin except for the frequent

appearance of a dotlike whitish necrotic layer on its summit, and not uncommonly this central or eccentric zone shows a tiny excavation following its traumatic removal. When lesions develop on the female genitalia they are larger, painful and tender and have a tendency to ulcerate. Dysuria is a common complaint when the eruption appears about the urethra. Buccal lesions sometimes leave scars on healing, but those on the genitals do so invariably.

Pustules develop either spontaneously or secondarily from papules. They correspond in size to papules, and the incidence of inflammatory areolas is likewise similar. Removal of their epidermal covering releases a small amount of light cloudy fluid and exposes a red, flat, excoriated surface, which sometimes contains a minute central or eccentric excavation.

Cycles of remissions and exacerbations are common regardless of treatment. During a relapse it is not unusual for the patient to feel and look perfectly well and even gain in weight. The eruption has a tendency to develop in areas of lowered resistance. In 1 patient numerous lesions appeared on the site occupied previously by a dermatitis due to adhesive tape while in another case great numbers of superficial papulonecrotic tuberculids were noted in an area occupied one month previously by an eruption of herpes zoster.

Not uncommonly a patient with superficial papulonecrotic tuberculid displays another type of cutaneous tuberculosis or tuberculous disease of other viscera. In my experience this eruption in the adult was seen coincidentally with the nodular form of papulonecrotic tuberculid, with erythema induratum, erythema nodosum, lupus erythematosus of the discoid type, tuberculous lymphadenitis, pleurisy with effusion, pulmonary tuberculosis, spontaneous pneumothorax, tuberculous tenosynovitis and arthritis.

Subjective symptoms fluctuate considerably in the adult. The patient may be entirely asymptomatic or severely ill. Indefinite pain in joints is a common complaint, and not infrequently there is a "rheumatic" history of many years' standing. Various degrees of secondary anemia are encountered. In a few of my cases unexplained fever was diagnosed only after the appearance of the cutaneous tuberculid. In the adult the prognosis is usually favorable, since associated tuberculous disease of vital structures is not the rule, but in the infant the reverse is true.

These patients are highly sensitive to old tuberculin, for they invariably react locally to an intracutaneous injection of 0.1 cc. of a one to a million dilution. Sometimes positive reactions are obtained with a dilution as high as one to a quintillion. The Negro responds to the infection with a higher degree of allergy than does the white patient, and yet the latter acquires a greater degree of true immunity.[1] There

is no relationship between the degree of allergy and the intensity or type of inflammation in the cutaneous lesion. Banal inflammatory infiltrates with absence of collagenous degeneration or necrosis were noted in lesions of persons who reacted strongly to tuberculin in dilutions as high as one to a quintillion. However, it is customary to find dermal and epidermal necroses in the presence of such degrees of sensitivity.

TREATMENT

The aim of therapy is to increase the patient's resistance and thus secondarily effect healing of active tuberculous foci responsible for the bacteremia. Caseous lymph glands probably act as reservoirs for bacterial dissemination.[2] Clinical cures have been reported when these foci, accessible to direct therapeutic attack, were eradicated.[3] Intracutaneous injections of tuberculin, even after prolonged use, have not proved entirely efficacious. This likewise applies to therapy with gold, bismuth and arsenic. Iron therapy for secondary anemia and intramuscular injections of liver extract supplemented with orally administered vitamins A and D and members of the B complex group have proved beneficial. A permanent cure was not observed in any case even though observations were continued for two to three years. Nevertheless, the patients showed a decided improvement in the general health, relapses were less frequent and the number of cutaneous lesions diminished with continuous treatment.

HISTOLOGIC STUDIES

Sections were studied from 22 cases (4 girls, 16 women and 2 men), and the following observations were recorded. In the superficial papulonecrotic tuberculid the pathologic alterations were similar qualitatively to those of the nodular variety and differed merely in being smaller in scope and in the fixation of the process to the superficial vessels of the skin. Furthermore, some lesions healed without residual atrophy or scarring, since collagenous degeneration or necrosis did not always supervene. With rare exception the inflammation was limited to the upper one fourth, or more often to the upper one half, of the cutis.

The site of the maximum and probably the initial reaction appeared at different levels in the upper part of the cutis, but it was most often noted in the papillae or coincidentally in both papillae and subpapillae. In several instances the maximum cellular response, limited to the mid-

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2 Auerbach, O.: The Progressive Primary Complex, Am. Rev. Tuberc. **37**:346 (March) 1938.

3. Wright, C. S., in discussion on Greenbaum, S. S.: Papulonecrotic Tuberculid, Arch. Dermat. & Syph. **16**:491 (Oct.) 1927. Irvine, H. G., and Turnacliff, D. D.: Tuberculous Lesions of the Skin with Active Foci, ibid. **30**:900 (Dec.) 1934.

cutis, enveloped and invaded varying numbers of hair follicles, some of which were in the process of destruction.

The capillaries of the papillae and subpapillae usually bore the brunt of the initial reaction. There were various degrees of vascular dilatation and of swelling and proliferation of their endothelial cells and of injury to their supportive tissues with subsequent extravasation of serum and red blood cells. On occasion thrombosis was noted in these vessels. In several instances minimal vascular reactions with little or no surrounding cellular infiltrate were observed in the deep cutis, and in sections from 1 case they were detected in the subcutis. In the last-mentioned instance the collagen of the subcutis also showed degenerative change.

Disintegration of the perivascular connective tissues of the upper part of the cutis was a familiar occurrence. The collagen sustained granular, hyaline or basophilic degeneration. It was not unusual for basophilic and granular changes to appear together in a single focus, while on other occasions granular and hyaline degeneration were noted in the same sections but at different levels.

The necroses were characterized by liquefaction, coagulation or caseous changes. The first two changes were often noted in the same focus. Caseous necrosis was found but once, and this was seen in the midcutis. The stroma bordering the necrotic area was either normal or more commonly edematous or in a state of degeneration.

Most sections showed a perivascular banal type of inflammation. The small lymphocyte was the chief cell type, but polymorphonuclear neutrophils were often seen in large numbers in the most intensely inflamed areas. In many instances the granulocyte was probably the first cell to respond to the initial insult. Tuberculoid structure was noted in several lesions which had been present for more than one week. This form of epithelioid cellular response was always seen in the midcutis, and it appeared to envelop hair follicles, some of which were partially or completely destroyed. Tubercle formation was lacking entirely, and giant cells were rarely present, and then only in relation to tuberculoid structure. Epithelioid cells, singly or in small groups, were frequently encountered in the dense lymphocytic infiltrate. There was a tendency for small round cells, polymorphonuclear neutrophils and red blood cells to invade the epidermis, and here they collected in greatest numbers in necrotic foci. Lesions showed early healing tendencies, for connective tissue proliferation about degenerative and necrotic foci in the cutis was often present in eruptions of but a few days' duration.

In the vast majority of sections the epidermis showed abnormal changes. Cellular proliferation and parenchymatous edema with or without subsequent necrosis were commonplace observations. The

severest grades of epidermal inflammation were always directly above similar degrees of inflammation in the uppermost layers of the cutis. Liquefaction necrosis was common. It varied in scope, at one extreme

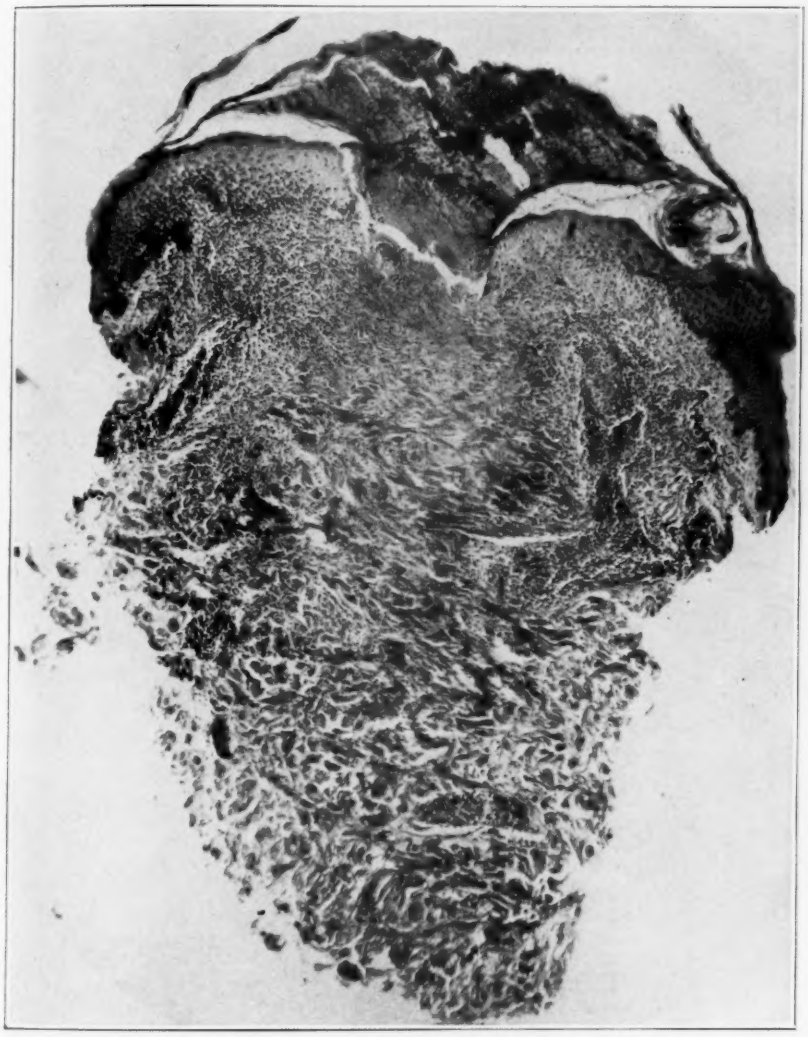

Fig. 3.—Note the small area of coagulation necrosis of the collagen of the papillae and subpapillae. The adjacent overlying epidermis is similarly affected. The outlying perivascular cellular infiltrate is of the banal type. (Hematoxylin and eosin; × 60.)

affecting a few basal cells and a few neighboring prickle cells while at the other extreme all cells of the epidermis were involved within a small circumscribed area. Coagulation necrosis was less frequent, and

Fig. 4.—A well defined zone of collagenous degeneration and necrosis may be seen in the upper one fourth of the cutis. The surrounding cellular reaction is of the banal type. Inflammation is absent below the midcutis. (Hematoxylin and eosin; × 60.)

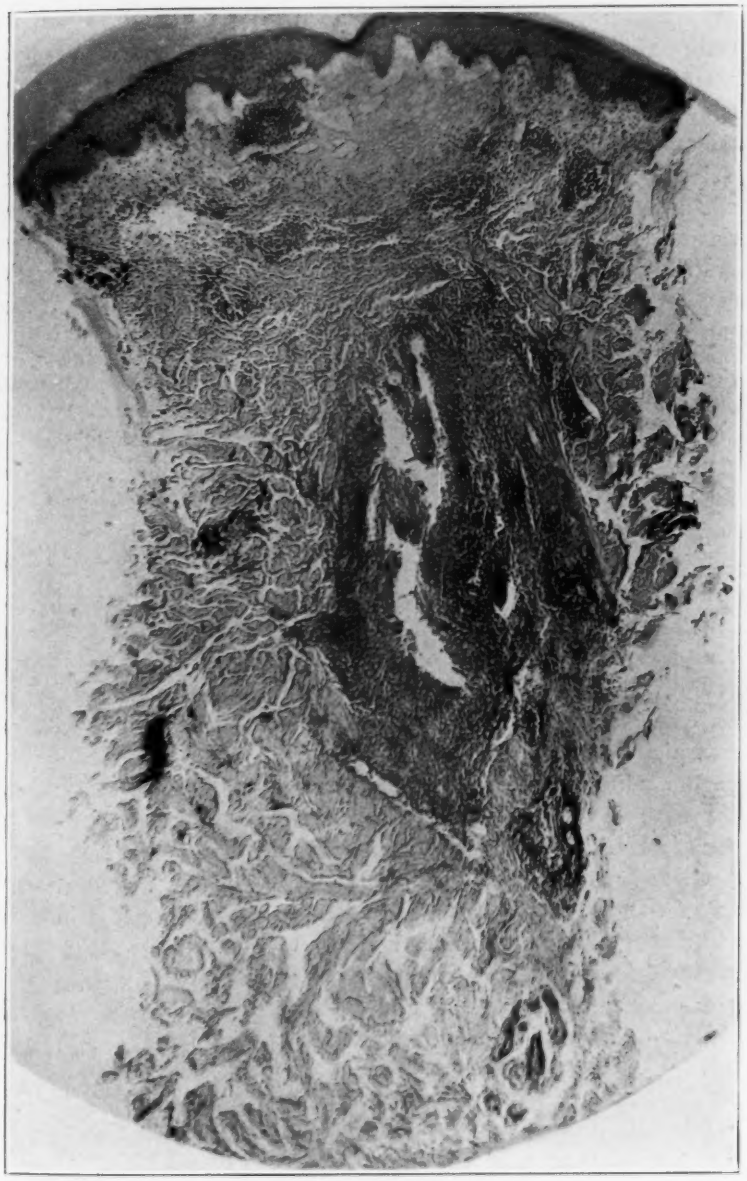

Fig. 5.—Note the oval zone of liquefaction and coagulation necrosis affecting the collagen of the papillae and subpapillae. Directly below is a large circumscribed perifollicular infiltrate, the lower border of which reaches the midcutis. The infiltrate is tuberculoid. Within this area the supportive tissue is destroyed and a single hair follicle is disrupted. There is no inflammatory reaction below the midcutis. (Hematoxylin and eosin; × 110.)

it usually affected the entire epidermal layer. It was practically always associated with a similar change in the connective tissues of the upper part of the cutis. Conversely, liquefaction of the collagenous tissues was not necessarily associated with a like change in the epidermis.

Obviously histologic study is of assistance for recognition of superficial papulonecrotic tuberculid, but in the absence of collagenous degeneration or necrosis or tuberculoid structure a microscopic diagnosis is impossible. In the absence of atrophic sequelae a clinical diagnosis is hazardous even if the patient demonstrates a high state of allergy to tuberculin. In cases in which the diagnosis is doubtful continued observation will undoubtedly substantiate a diagnosis of superficial papulonecrotic tuberculid, for typical microscopic and clinical features develop ultimately.

SUMMARY AND CONCLUSIONS

Tuberculids occur more frequently in the Negro than in the white patient, and the papulonecrotic tuberculid is the most common type.

In the Negro the superficial papulonecrotic tuberculid is seen more often than the nodular type, although both forms may develop concurrently in the same locality.

Clinically, superficial papulonecrotic tuberculid may simulate acne vulgaris, keratosis pilaris, secondary syphilid, papular urticaria, varicella, iododerma or bromoderma.

The Negro with papulonecrotic tuberculid is highly sensitive to tuberculin. A positive local reaction is practically always obtained with 0.1 cc. of a one to a million dilution and in some instances with dilutions as high as one to a quintillion.

In the adult Negro papulonecrotic tuberculid is a more serious disease than in the white patient, because complicating tuberculous disease of other viscera is seen more often in the former.

A clinical cure was not seen in any case even after an observation period of two to three years. However, the patients show invariably a decided general improvement in addition to a lessened tendency toward relapses and fewer cutaneous lesions in subsequent recurrences.

The clinical characteristics and microscopic changes of superficial papulonecrotic tuberculid are discussed.

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PROPERTIES OF HUMAN SKIN REVEALED BY FLUORESCENCE MICROSCOPY

III. PARAFFINOMA

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In a previous communication [1] we described the appearance of the normal skin under the fluorescence microscope as the basis for histologic studies of the skin. In addition, we referred to the visualization of vitamin A by this method.

We have studied the appearance of cutaneous sections made from paraffinoma tissue. The histologic picture was as follows: The epidermis was in all respects similar in appearance to that of normal skin. There were round and oval cavities scattered irregularly through the cutis and in the subcutis. These spaces varied considerably in size and presented the well known Swiss cheese picture found in paraffinoma. Whereas with ordinary staining methods these spaces appear clear and transparent, under the fluorescence microscope they were a vivid turquoise blue. Their color was homogeneous within each cavity, though the smaller ones showed a more intense color. Their color did not change on continued ultraviolet irradiation. No especial characteristic was shown by the surrounding connective tissue. The elastic tissue was increased in quantity, but particularly by hyperplasia of individual fibers. Well demarcated areas of hypertrophy were seen especially in the upper half of the cutis and sometimes well away from any of the lakes. Only occasionally the areas of hypertrophied elastica extended down to the subcutis, where the lakes were largest. The fluorescence of the connective tissue and of the fat was the same as that seen in normal skin. The vitamin A fluorescence likewise was the same as that seen in normal skin. The lakes did not impart any vitamin A fluorescence.

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1. Cornbleet, T., and Popper, H.: Properties of Human Skin Revealed by Fluorescence Microscopy: The Normal Skin; the Vitamin A Content of the Skin, Arch. Dermat. & Syph. **46**:59 (July) 1942.

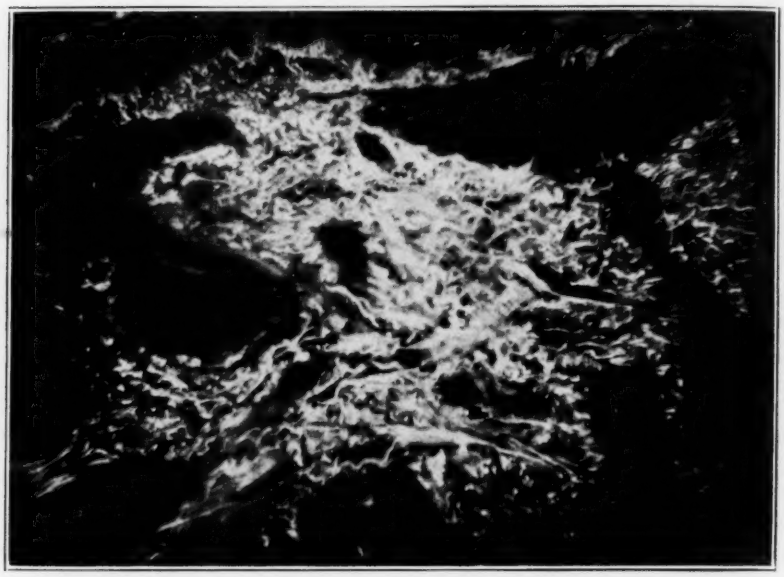

Fig. 1.—Photomicrograph of the skin (low power magnification), showing extensive proliferation of the elastic fibers and membranes characterized by bright nonfading gray fluorescence. The foci of elastica proliferation are seen in the subpapillary layer and around hair follicles.

Fig. 2.—Photomicrograph of the skin (low power magnification), showing clearly the bright fluorescent elastic network. The fluorescence of the lakes is not bright enough to contrast sufficiently in black and white; color photography does record this contrast.

SUMMARY

1. The paraffin lakes in sections of tissue from paraffinomas examined under the fluorescence microscope are seen to emit a vivid turquoise blue color.

2. The elastic tissue is hypertrophied (the individual fibers) and imparts its usual brilliant color.

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COMBINED VACCINE AND TOXOID THERAPY OF STAPHYLOCOCCIC INFECTIONS OF THE SKIN

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In the experimental animal staphylococcus antitoxin increases the resistance of the skin against the necrotizing power of staphylococcus toxin (anatoxin). That this dermonecrotic action in man may also be neutralized by antitoxin is borne out by observations such as those of Stookey and Scarpellino.[1] The latter obtained a cure in 3 out of 6 cases of staphylococcic septicemia with necrosing cutaneous lesions by means of injections of staphylococcus antitoxin. In the common varieties of coccogenous dermatoses in which the staphylococcus plays a primary or secondary role it has never been satisfactorily proved that the clinical and pathologic picture can, in whole or in part, be accounted for by formation of toxin. The good results reported in the treatment of such infections by means of subcutaneous injections of increasing doses of staphylococcus toxoid (toxin detoxified with solution of formaldehyde) have ordinarily been attributed to an augmented antitoxic titer in the blood. Dolman,[2] in originally reporting the rapid cure of 16 patients with severe pustular acne and a few miscellaneous staphylococcic infections, claimed to have obtained in every case an appreciable increase in antitoxin units in the blood after the first three or four injections. He was inclined to attribute his good results to such active immunization in spite of the fact that he did not note any correlation between the type or severity of the clinical infection and the capacity of the causal organism to produce toxin in vitro. Excellent clinical results in furunculosis and acne following a rapid increase in antitoxin units in the blood were noted by Ramon, Bocage, Richou and Mercier.[3]

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† Dr. Goodman died on Oct. 26, 1942.

1. Stookey, P. F., and Scarpellino, L. A.: Specific Treatment of Staphylococcic Infections of the Skin, Arch. Dermat. & Syph. **36**:106 (July) 1937.

2. Dolman, C. E.: Treatment of Localized Staphylococcic Infections with Staphylococcus Toxoid, J. A. M. A. **100**:1007 (April 1) 1933.

3. Ramon, G.; Bocage, A.; Richou, R., and Mercier, P.: Sur l'immunité antistaphylococcique provoqueé por l'anatoxine spécifique chez les malades atleints d'affections duesau staphylacoque, Presse méd. **44**:281, 1936.

On the other hand, Kindel and Costello,[4] employing a toxin derived from a good toxin-producing Burky strain of staphylococcus and detoxified with a dilute solution of formaldehyde U. S. P. (0.3 per cent), could not duplicate these results. Of their series of 28 cases of acne (in 22 of which the lesions were pustular), 8 of sycosis vulgaris and 6 of furunculosis, a total of 42 cases, in 8 the condition was slightly improved and in 34 it was unimproved or worse at the end of treatment. The average number of treatments administered was nine and four tenths and the average total dosage of toxoid 6.11 cc. These authors did not give figures of increased antitoxin titer, but the number of injections and the dosage of toxoid were comparable to those of the aforementioned investigators. Dolman,[5] in a later report, expressed less optimism in regard to results achieved but felt that very poor results could be ascribed to the use of an antigen of low toxic unitage.

The conflicting results obtained with the use of toxin and toxoid have raised several questions. Although injections of increasing doses usually augment the antitoxic units in the blood, it is probable that the immune bodies often fail to reach the skin in sufficient quantity to neutralize the free toxin. Poor results might be due, as Dolman suggested, to the use of a weakly antigenic toxoid. There is, furthermore, no definite knowledge as to whether in other than frankly necrotizing processes the clinical and pathologic phenomena are brought about by staphylococcus toxin. It is safe to assume that the common varieties of staphylogenous dermatoses, including pustular acne, are not dependent entirely on the action of toxin or the lack of production of antitoxin. It has been found that sometimes a patient with a good serologic increase in staphylococcus antitoxin titer in response to injections of toxoid showed poor clinical results, whereas one with a poor serologic response did well.[6] In my series 1 patient with severe sycosis vulgaris, who had a reading of 7 units of staphylococcus antitoxin per cubic centimeter of serum at the commencement of treatment, showed considerable clinical improvement after a course of ten injections in spite of the fact that at this point his blood gave a reading of less than 0.1 unit of antitoxin per cubic centimeter. This reduction in antitoxic titer might be explained on the basis of an exhaustion of the ability to react. On the other hand, the clinical improvement in such a case could be due to specific desensitization brought about by the metabolic products of the organisms.

4. Kindel, D. J., and Costello, M. J.: Staphylococcus Toxoid in the Treatment of Pustular Dermatoses, J. A. M. A. **102**:1287 (April 21) 1934.

5. Dolman, C. E.: Staphylococcus Toxoid in the Treatment of Pustular Dermatoses, Correspondence, J. A. M. A. **102**:1699 (May 19) 1934.

6. Fleming, A.: Recent Advances in Vaccine Therapy, Brit. M. J. **2**:99, 1939.

Allergic hypersensitivity to the metabolic products of the staphylococcus undoubtedly plays a greater or lesser role in cutaneous infections due to this organism.[7] Cathala and Auzepy [8] stressed the benefits of specific shock or desensitization effects from the toxin-containing filtrates or from the vaccine suspensions of staphylococci.

It is understood that detoxified staphylococcus toxin (toxoid) as commonly prepared contains many of the metabolic products of the organism. However, to assure a high content of these, capable of maximum allergenic effects, it was desirable to have available for clinical use a preparation which combined staphylococcus toxoid of high potency with a bacterial vaccine.[9] Anderson and Stokes treated a series of 84 patients with a multiple strain staphylococcus toxoid combined with bacterial antigen and concluded that it is a useful adjunct in the treatment of resistant pyogenic dermatoses.[10] Such a combined staphylococcus toxoid-vaccine when used for a sufficiently long time and in a sufficient number of doses, it was felt, would permit a reasonable estimate of the value of antitoxic and desensitizing effects of this type of therapy in the common staphylodermas.

METHOD AND PATIENTS TREATED

All injections were given into the deltoid muscle, alternating left and right. With an initial injection of 0.1 cc. the dose was increased by this amount at each treatment, which was given every fourth day until the patient received the tenth injection, of 1 cc. These ten inoculations were considered as one full course.

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7. Sulzberger, M. B.: Dermatologic Allergy, Springfield, Ill., Charles C Thomas, Publisher, 1940, p. 337.

8. Cathala, J., and Auzepy, P.: Sur le traitement des staphylococcies; questions de doctrine, Arch. de méd. d. enf. **41**:711, 1938.

9. (*a*) The antigen employed in this study was supplied in 5 cc. vials under the name of Va-Tox (National) by the National Drug Company. It was described as a polyvalent staphylococcus vaccine (Staphylococcus aureus 2,000 million per cubic centimeter) combined with a standardized staphylococcus toxin, detoxified with formaldehyde to form a toxoid (staphylococcus toxoid-1,000 original M.N.D. per cubic centimeter). (*b*) Experimental evidence was brought to my attention indicating that a preparation of this type when injected into animals effectively increased both agglutinins and antitoxin to a greater degree than in control animals which were immunized with staphylococcus toxoid or vaccine separately (Etris, S.: Study of Antigenic Properties of Combined Staphylococcus Vaccine and Toxoid, to be published).

10. Anderson, L. E., and Stokes, J. H.: Staphylococcus Ambotoxoid: Experience with Its Use in the Treatment of Acne Vulgaris and Other Pyogenic Dermatoses, Arch. Dermat. & Syph. **40**:382 (Sept.) 1939.

The total number of patients treated and observed sufficiently to draw conclusions were 105. The following list indicates the number treated in each group:

Pustular, nodulopustular (including cystic) acne	46
Chronic blepharitis	3
Sycosis vulgaris	5
Acne varioliformis	3
Hidradenitis suppurativa	10
Recurrent styes	10
Furunculosis	10
Recurrent localized subcutaneous infections of buttocks and thighs	7
Chronic suppuration of subcutaneous tissue (buttocks)	1
Folliculitis keloidalis	2
Infectious eczematoid dermatitis	5
Rosacea with nodulopustulation	1
Refractory pustular dermatosis of hands and feet	2

Although determinations of the quantity of antitoxin in the blood were made too infrequently to warrant recording, it was suggested that in essentially acute processes, such as an attack of styes or infectious eczematoid dermatitis, the possible increase in antitoxin units was responsible for rapid beneficial effects. This point is borne out by the fact that in most of the 15 cases of these two groups there was a favorable response to only three or four injections of the combined antigen. The styes were all of the recurrent type, and none of the 10 patients suffered a relapse during at least eight months following a full course of ten injections. In all 5 cases of infectious eczematoid dermatitis the condition had been stubborn, but it responded rapidly when the injections were given in addition to the local treatment.

In conformity with the concept of desensitization in the chronic and recurrent staphylogenous conditions, treatment was continued with the antigen in 1 cc. doses at four day intervals or at weekly intervals after the completion of the routine single course.

In 1 case chronic blepharitis (associated with folliculitis of the nasal vestibule) cleared up completely after fifteen such injections of 1 cc. each were given following the initial course of ten injections. In the 2 remaining cases, in 1 of which there was a local and systemic reaction, the condition was merely improved after twenty such injections. The antigen is to be credited with the cure of the 5 patients with sycosis vulgaris. One of these was a Negro who responded after a single course. Two other patients received respectively five and ten 1 cc. injections after the initial course. The fourth patient was the one referred to previously, who responded in spite of a decreasing quantity of antitoxin in the blood. This patient received, including the initial

course, a total of twenty-six injections. The fifth patient continued to remain free from lesions five months after an initial course. One patient with acne varioliformis responded and had shown no recurrence one year after receiving the single course. Another patient responded after the initial course of ten injections but relapsed three months later. The third patient had not suffered an attack for six months after receiving a series of sixteen injections. Nine of the 10 patients with hidradenitis suppurativa, all treated in the incipient stage of the disease, responded favorably after five to ten injections of the initial course. Suppuration was forestalled in all these in spite of the use of hot fomentations to relieve pain. Eight patients with persistent furunculosis showed excellent results with ten to fifteen injections including the initial course. One of these sustained a severe local and systemic reaction, which will be discussed in another part of this paper. Two patients with furunculosis were not benefited by fifteen injections each. Seven patients who suffered with recurrent single or multiple localized and circumscribed staphylococcic infections of the buttocks and thighs were treated. Such painful subcutaneous inflammatory lesions may complicate a simple folliculitis or result directly from irritation of excessive sweating, friction or other injury, especially during the summer months. Lesions of this type usually go on to suppuration. Six of these patients were completely relieved by the initial series of ten injections and also avoided the suppuration which had formerly required repeated incision and drainage. One patient was not influenced by the treatment. As indicated in the list, the material was tried on a patient whom I had observed for several years for a chronic suppurative process in the subcutaneous tissue of both gluteal regions. Although a cure was not obtained the condition did become essentially quiescent after a total of twenty-five injections, including the initial course. Two patients with folliculitis keloidalis received fractional roentgen therapy concomitant with the initial course of the antigen. Both of these patients were cured and showed no recurrence after one year. A 24 year old woman with a long-standing severe rosacea associated with recurrent deep-seated nodulopustular lesions had not responded to fractional roentgen therapy and local applications. Striking improvement and complete arrest of the tendency to nodulopustulation took place after sixteen injections, including the initial course. There was no relapse in fourteen months. Two patients with refractory pustular dermatosis of the hands and feet showed decided improvement after fifteen and sixteen injections, including the initial course. However, 1 patient continued to show at longer intervals a few pustules on the feet but rarely on the hands, and the other had no attacks on the hands for eight months following the termination of treatment.

TREATMENT OF ACNE

In this study many of the patients were selected for treatment only after the usual measures, including roentgen therapy (where indicated), had been used with partial or complete success and relapse had occurred. On the other hand, some patients in the group with acne were included who had received no previous formal therapy for a severe pustular type, commonly recognized as recalcitrant to accepted forms of therapy. Patients with ordinary acne of the comedo type with or without papulopustulation were not included in this series. Those treated had the chronic pustular and cystic variety in which there is little tendency to the development of comedos. It would seem that if the staphylococcus is at all causative in this type of acne the chronicity and tendency to acute exacerbations suggest an allergic hypersensitivity of the tissues to this organism and its exotoxin rather than an ineffectively low antitoxin content of the blood. Since most of the patients were from

Results of Treatment of Patients with Pustular, Nodulopustular (Including Cystic) Acne Vulgaris with Combined Staphylococcus Vaccine and Toxoid*

Number of Patients	Unimproved	Slightly Improved	Moderately Improved	Greatly Improved †	Apparently Cured ‡
46	2	3	3	12	26

* Every patient was observed for at least fifteen months following the last injection.

† "Greatly improved" means that the skin remained relatively free from active lesions with or without the continued use of simple local and general measures.

‡ "Apparently cured" means that the skin remained absolutely free from active lesions with or without the continued use of local and general measures.

private practice some concomitant therapy, which hitherto had in itself produced no substantial effects, had to be given. This included instructions as to regularity in habits of eating (balanced diet), elimination, rest and exercise and the use of a mild sulfur lotion.

For purposes of possible desensitization the patients in this acne group were given continuous treatment with the antigen in 1 cc. doses at four day intervals after they had completed the initial course. A few of the patients received only five of these additional injections, but a larger number of them received as many as fifteen. Three of the patients who would have been placed in the group designated in the table "Greatly Improved" when they had received a total of fifteen injections of 1 cc. each merited being placed in the group designated "Apparently Cured" after receiving an additional five injections. All of the patients were observed for at least fifteen months following their initial course of ten injections.

REACTIONS

All patients had some local reaction at the site of the initial injection, marked by tenderness, with or without erythema and extending over

an area from 1 to 2 inches (2.5 to 5 cm.) in diameter. Subsequent injections produced much less reaction, even with the repeated 1 cc. doses. Severe reactions, both local and constitutional, were observed in only 2 cases of the entire series. One was that of a robust man suffering with a combined (previously refractory) hidradenitis of the right axilla and furunculosis of the back of the neck. Eighteen hours after an initial injection of 0.1 cc. intramuscularly, chills, fever (temperature of 101 F.), malaise, muscular weakness, anorexia and headache developed with a local reaction of intense edema and erythema involving the entire arm. He was bedridden for three days. Injections were resumed with 0.025 cc., and this dose was increased by an equivalent amount at four day intervals. He continued to suffer some sense of weakness, but there was remarkable improvement of the coccogenous processes, which quickly abated and then gradually cleared up over a period of six weeks. In the second case of reactions there were mild constitutional symptoms with local reaction but no chills or fever. In this case stubborn blepharitis of the left lower eyelid became arrested but not cured. No serious reactions were encountered.

SUMMARY AND CONCLUSIONS

1. It is not known whether the exotoxins or the metabolic products of the staphylococcus are responsible for the pathologic reactions in patients with infections of the skin produced by this organism.

2. Clinical experience suggests a possible allergic hypersensitivity to the toxin or/and the bacterial products as causative.

3. There is a sound basis for the use of a combination of staphylococcus vaccine with toxoid to obtain not only an agglutinin in addition to an antitoxin response but also a potent allergenic effect for possible desensitization.

4. One hundred and five patients with various types of staphylodermas (including 46 with pustular acne) were treated with a combined toxoid-vaccine antigen. Injections were given in increasing doses every fourth day until the tenth dose, of 1 cc. In the usually refractory types of infection, such as pustular acne, treatments were continued in 1 cc. doses with the object of achieving desensitization.

5. By means of this desensitizing regimen it appeared that most of the patients were benefited and a great number obtained what may be justifiably considered a clinical cure.

6. The results of this study are promising and warrant the trial of combined staphylococcus toxoid and vaccine as an adjunct in the treatment of some of the ordinarily stubborn staphylococcic dermatoses.

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EPIDERMOLYSIS BULLOSA

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AND
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Epidermolysis bullosa, sometimes described as acantholysis bullosa, a somewhat rare dermatosis, is of considerable interest. This hereditary disease is uncommon in civilian practice. In military life, especially with the careful selection of members of the armed forces, it is most rare. Recently, 4 soldiers were admitted to Lawson General Hospital, Atlanta, Ga., complaining of this rare dermatosis. Two of these had the hereditary type and 1 the acquired type. The fourth had a rare hereditary type with the bullae limited to the feet. Cockayne [1] described this type in the *British Journal of Dermatology* in 1938. No case of this type has previously appeared in the American literature.

REPORT OF CASES

CASE 1.—S. J., an unmarried American aged 24, was seen in July 1942. According to his history, his grandfather and father suffered from the same defect. His 2 brothers were not afflicted. Three of his 6 sisters had similar changes. Of a total of 5 nephews 3 showed similar changes, and of a total of 9 nieces 5 were afflicted. The remaining members of the family have been unaffected.

The patient was transferred to this hospital for treatment of a recurring eruption of the feet which had developed shortly after birth. Since birth he had not been completely free from lesions for any prolonged period. He stated that he had had vesicles and bullae of varying sizes occurring on his feet and hands. Bullae had occurred on many parts of his body that were rubbed thoroughly or traumatized. He never had any lesions in the mouth, and the only complaint that he had at present was a burning sensation of both feet. Although the eruption appeared at any time, it was more pronounced in the summer season. He found the wearing of shoes difficult, and sometimes he was unable to work.

Examination of the skin showed many deep-seated bullae about 1 to 2 cm. in diameter distributed symmetrically on both soles. A few discrete bullae were present over the achilles tendon. There were numerous fine milia on the upper part of the back. Laboratory data were unimportant. The Wassermann reaction of the blood was negative and the blood count normal. Bacteriologic and mycologic study of material from the lesions did not disclose any organisms.

CASE 2.—H. E., an unmarried American aged 37, was seen in July 1942. According to his history, his grandfather and father had the same defect. He

1. Cockayne, E. A.: Recurrent Bullous Eruption of the Feet, Brit. J. Dermat. **50**:358, 1938.

had 1 brother who was afflicted. One of his 3 sisters had similar changes. A niece, the child of a brother, was likewise afflicted.

He was transferred to this hospital for treatment of a recurrent eruption of the feet which had developed shortly after birth. As in case 1, this patient stated that he had had the eruption on his feet, his hands and, occasionally, his body as long as he could remember. Since early childhood he had not been completely free from the eruption for any prolonged period. The bullae might occur spontaneously or appear after rubbing or traumatizing the skin. There were no subjective complaints with the exception of a slight burning sensation. There were no lesions in the mouth or on any other mucous membranes. He also stated that his eruption was worse in the summer and found that the wearing of shoes increased his difficulties.

The usual laboratory data were unimportant. The Wassermann reaction of the blood was negative and the blood count normal. Bacteriologic and mycologic study of material from the lesions did not disclose any organisms.

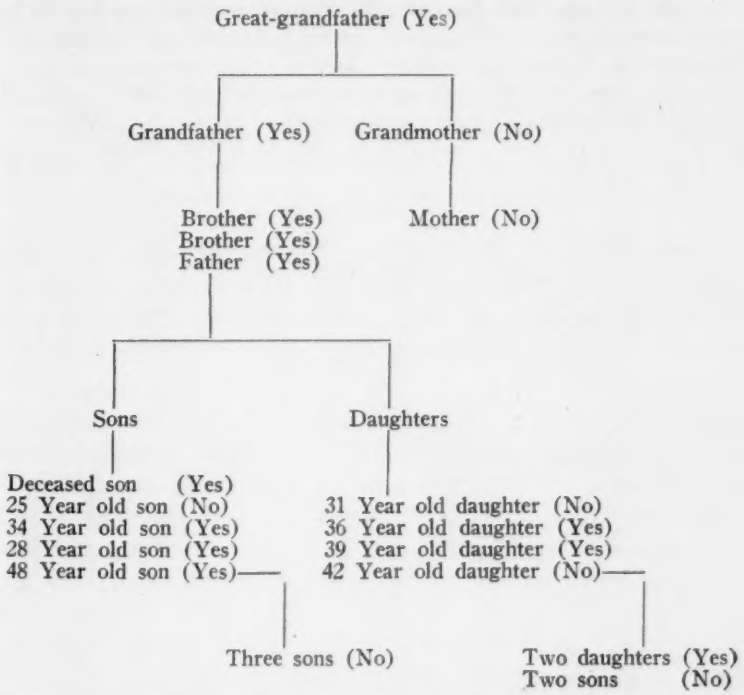
CASE 3.—N. E., an unmarried American aged 23, was seen in October 1941. According to him, there was no history of chronic recurrent eruption in his family or relatives. He was transferred to this hospital originally with a diagnosis of sciatica. It was noticed that he had an eruption on his feet, which he said had kept recurring over a period of five years. Since its inception, there had been no prolonged periods in which he had been free from lesions. He had been treated for a fungous infection and for contact dermatitis during these five years. Wet dressings had little effect on the course of this eruption. Relief was obtained only by staying off his feet and avoidance of wearing shoes. He had no subjective symptoms. This patient was under our observation and care for ten months. At no time was he completely free from lesions.

On examination of the feet there were a number of bullae of varying sizes. Some were on the soles and heels; others were on the toes, on the dorsa of the feet and over the achilles tendon. The bullae were gray and tense. They appeared after mechanical irritation or slight trauma due to pressure from shoes. The blebs healed without leaving scars or pigmentation. There was no permanent alteration in the skin. There was no evidence of an inflammatory reaction. There was no eruption on any other part of the body. All treatment to date has been of no avail. Because of the clinical picture and course of this recurrent bullous eruption, a diagnosis of acquired epidermolysis bullosa (simple form) was made.

Histologic examination was made by Dr. Charles Sims. The epidermis was fairly regular. The rete pegs were moderately elongated and in some places club shaped. There was a fairly well defined granular layer throughout most of the section. The center of the section presented a separation of the epidermis from the underlying cutis at the dermal-epidermal junction. At some points one might note where the papillary bodies had separated from corresponding positions in the overlying epidermis. The space formed between epidermis and cutis was filled by a fibrinous fluid, with few cellular elements contained therein. Within the papillary zone there was a diffuse cellular infiltration. It was composed of small round cells and wandering connective tissue cells. The vessels of the upper part of the cutis and of the midcutis were moderately dilated.

CASE 4.—C. F., an unmarried American aged 28, was seen in February 1942. According to his history, his great grandfather, grandfather and father had the same cutaneous defect. Two of his uncles on his father's side had a similar

disease. The patient had 3 brothers, of whom 2 had similar changes; a deceased brother also had had a similar condition. Of 4 sisters, 2 were similarly diseased. The patient had 5 nephews who were free of the lesions but 2 nieces who had similar involvement. He sought treatment for a recurring eruption on the feet which developed shortly after birth. He had never been free from it for any prolonged period. Although the eruption appeared in any season, it was usually worse in the summer, when increased perspiration increased the frequency and discomfort. The patient found it exceedingly difficult to wear shoes, so that at times he could not carry on his work. The only subjective symptoms were pruritus and discomfort, which varied with the extent of the lesions. The lesions were located on the flexor surfaces of the feet, usually bilaterally.



According to the patient, a blister of varying size would appear, which soon ruptured but did not spread peripherally. After a few days the lesions would gradually disappear but did not become crusted. Many topical preparations had been used, some of which gave palliative relief. He found that wet dressings of physiologic solution of sodium chloride or solution of aluminum acetate N.F. reduced the discomfort but did not alter the progress of the disease or tend to dry up the lesions. The eruption disappeared spontaneously in seven to eight days, only to reappear somewhere else on the feet. Occasionally the new lesion would reappear on the site of the preceding lesion. The patient stated that his father and many of his relatives, including his brothers and sisters, had similar eruptions persisting during their lifetime. They stated that the lesions were kept to a minimum by wearing shoes with stiff soles and also by definite limitation of walking. There was no other cutaneous eruption or any history of drug taking.

Examination of the patient over the past four months confirmed his description of the previous occurrences. The lesions varied in number and size. The bullae were grayish and tense to the touch and appeared rather thick. The patient seldom was free of the eruption. As many as twenty lesions would be present at one time; some were pea sized and others half the size of an English walnut. These lesions were discrete and did not coalesce. When they disappeared, there was occasionally a small pigmented area, probably due to a deposit of hemosiderin. There was no residual scarring or pitting, nor was there any evidence of excoriation or adenopathy. Sometimes the skin of the toes was involved; at other times the integument of the whole foot was affected. Nikolsky's sign was not elicited.

Laboratory data were unimportant. The Wassermann reaction of the blood was negative. The blood count was normal. Bacteriologic and mycologic study of material from the lesions did not disclose any organisms.

Sections from the skin of the foot revealed a definite cleavage of the epidermis with a serous exudate. There was considerable loss of elastic tissue when appropriate stains were used. There was no evidence of subepithelial scarring.

SUMMARY

Four cases of epidermolysis bullosa occurring in soldiers are described. The clinical and histologic pictures are presented. A case of acquired epidermolysis bullosa is reviewed. One case of the bullous eruption limited to the feet, as described by Cockayne, is reported.

VITAMIN B_6 (PYRIDOXINE) IN DERMATOLOGY

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There are still many questions about vitamins that remain unanswered, although thousands of research workers and clinicians are giving considerable attention to their study. The medical literature is literally swamped with publications on vitamins, and it is with hesitation and mental reservations that an additional article is added, even after a two year study.

Little is known concerning the exact role of vitamin B_6 (pyridoxine), which is only a small branch on the ever growing vitamin B complex tree, but the isolation of vitamin B_6 was announced only in 1938 by Keresztesy and Stevens.[1] Physiologic activity in acrodynia of the rat was first described by Antopol and Unna.[2] Of considerable significance were the studies of Sullivan and Nicholls,[3] who made the following observations: "In rats fed a basal vitamin B free diet supplemented with thiamin, riboflavin, nicotinic acid and filtrate factor, but completely devoid of vitamin B_6, there developed a symmetric dermatitis. The sites involved were the dorsa and plantae of the paws, the nose, the lips, the chin, the submental region, the upper chest and occasionally the sides of the face."

Our interest in pyridoxine was first stimulated by the report of Spies, Bean and Ashe[4] on 4 patients with pellegra who had failed to recover entirely on a selected diet with supplements of thiamine,

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The vitamin B_6 used in this study was furnished by Merck & Co.

Presented as part of the Panel Discussion on Vitamins at a meeting of the Academy of Dermatology and Syphilology, New York, Dec. 16, 1941.

1. Keresztesy, J. C., and Stevens, J. R.: Crystalline Vitamin B_6, Proc. Soc. Exper. Biol. & Med. **38**:64 (Feb.) 1938.

2. Antopol, W., and Unna, K.: Pathology of Vitamin B_6 Deficiency in the Rat and Response to Treatment with Vitamin B_6, Proc. Soc. Exper. Biol. & Med. **42**:126 (Oct.) 1939.

3. Sullivan, M., and Nicholls, J.: The Nutritional Approach to Experimental Dermatology; Nutritional Dermatoses in the Rat: I. Vitamin B_6 Deficiency, J. Invest. Dermat. **3**:317 (Aug.) 1940.

4. Spies, T. D.; Bean, W. B., and Ashe, W. F.: A Note on the Use of Vitamin B_6 in Human Nutrition, J. A. M. A. **112**:2414 (June) 1939.

riboflavin and nicotinic acid but who responded favorably to a single 50 mg. dose of vitamin B_6. Therapy with pyridoxine was immediately given to a patient with pellagra at Temple University Hospital in whom no response had followed the usual therapeutic procedures, and the improvement was almost immediate in cutaneous lesions, which were the predominant manifestations.

CLINICAL USES (DERMATOLOGY)

The results of animal experimentations indicated possibilities in the application of vitamin B_6 therapy to the treatment of diseases of the skin in man, and Spies, Bean and Ashe were the first to discover any definite clinical use. Paul Gross [5] suggested the necessity of investigating the effect of therapeutic doses of pyridoxine (and pantothenic acid) on cutaneous manifestations due to deficiency of factors of the vitamin B complex other than thiamine, riboflavin and nicotinic acid (Gross's therapy was limited to liver extract only). Smith and Martin [6] reported efficacy of vitamin B_6 in 3 of 4 cases of cheilosis.

The patients studied by us included persons with seborrhetic dermatitis, atopic eczema with seborrheic features and eczematous eruptions of unknown cause. Many of our patients had received previous therapy (with ointments, pastes, lotions, ultraviolet radiation and roentgen rays) with little or only temporary benefit. Patients were permitted to continue their previous therapy, but in most instances no other treatment was given except injections of pyridoxine in 25 to 100 mg. doses.

The efficacy of vitamin B_6 therapy was gaged by: (1) improvement noted subjectively by the patient, (2) clinical objective observations (disappearance of the lesions and return of the skin to normal) and (3) results of laboratory tests (the colorimetric method of Scudi, Unna and Antopol,[7] with which the need of the system for vitamin B_6 is determined by interpreting fluctuations in the concentration of the vitamin in the urine).

RESULTS AND CONCLUSIONS

A detailed report of the individual cases studied seems superfluous, since close controls were impossible and the possibility of spontaneous improvement could not be eliminated. The immediate response in a great many patients following the injections of vitamin B_6 was so striking that the patients expressed amazement. Other patients with iden-

5. Gross, P.: Non-Pellagrous Eruptions Due to Deficiency of Vitamin B Complex, Arch. Dermat. & Syph. **43**:504 (March) 1941.

6. Smith, S. G., and Martin, D. W.: Use of Vitamin B_6 in the Treatment of Cheilosis, Proc. Soc. Exper. Biol. & Med. **43**:660 (April) 1940.

7. Scudi, J. V.; Unna, K., and Antopol, W.: A Study of the Urinary Excretion of Vitamin B_6 by a Colorimetric Method, J. Biol. Chem. **135**:371 (Sept.) 1940.

tically similar clinical appearances showed little or no response. The corollary pointed out by Gross, that many patients with a seborrhea-like dermatitis show a definite but incomplete improvement with liver therapy, is true also in the case of injections of pyridoxine. In fact, we surmise that the vitamin B_6 content of liver extract may account for the therapeutic response in patients with certain eczemas following injections of liver. Gross stated: "The critical obstacle is that there is no direct means of determining vitamin B complex deficiency in a patient." The attempt to overcome this by quantitative estimation of the substance in urine (Scudi, Unna and Antopol) did not prove uniformly enlightening in our series of cases, yet it opens an avenue for the continued study of the utilization of the drug.

Clinically, the administration of vitamin B_6 resulted in definite improvement and occasionally in complete disappearance of seborrheic or seborrhoid eruptions when other standard measures failed. These observations disclose efficacy of the drug if not as a specific at least as an adjunct to other therapy. Our findings suggest that if vitamin B complex therapy is to be of definite value in the treatment of dermatoses of the seborrheic or eczematous type, the pyridoxine content must be adequate.

Several points of contention remain unanswered. Does the antidermatitic potency of vitamin B_6 rest solely in vitamin B_6 or in a combination with other factors? Are the tests for urinary excretion sufficiently reliable to estimate the necessity for or the utilization of pyridoxine? In what dermatologic entities can vitamin B_6 be of most value?

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CUTANEOUS ERUPTIONS DUE TO CODEINE

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Codeine has been widely used as a narcotic for over fifty years. In 1832 it was extracted from opium, and in 1881 its chemical formula was determined to be the methyl ester of morphine.[1] Nevertheless, eruptions due to hypersensitivity to this drug are very rare.

In the publications of Lewin (1882),[2] Morrow (1887)[3] and Kleeberg (1934)[4] on drug eruptions, codeine is not even mentioned. Bardet (1874),[5] studying the effect on himself of codeine and morphine in large doses, found this drug responsible for itching and erythema. This reaction, however, was due to overdosage rather than to hypersensitivity.

The first case of hypersensitivity to codeine was reported by Pollak in 1893.[6] A child of 1½ years ingested 0.002 Gm. of codeine daily, and after a few days pinhead-sized papules on a red base developed on the face and on the upper part of the thorax. This eruption disappeared after the withdrawal of the drug. In 1894 von Essen[7] reported the first scientifically established case. A woman of 31 years received codeine in a cough mixture and soon afterward there appeared an erythema on the arms, trunk, abdomen, inner sides of the thighs and knees associated with slight pruritus. The eruption disappeared a few days after the codeine was removed from the cough mixture. Later the patient was given 0.002 Gm. of codeine, and within three hours erythema and itching developed on the entire body with the exception of the face. The eruption disappeared four days later, leaving some desquamation. Further

From the Department of Dermatology, Kupat Cholin Polyclinic.

1. Kobert, E. R.: Lehrbuch der Pharmakotherapie, ed. 2, Stuttgart, Ferdinand Enke, 1908, p. 479.

2. Lewin, L.: The Incidental Effects of Drugs, translated by W. T. Alexander, New York, William Wood & Company, 1882.

3. Morrow, P. A.: Drug Eruptions, New York, William Wood & Company, 1887.

4. Kleeberg, L., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1934, vol. 4, pt. 2.

5. Bardet, G.: Etude physiologique et clinique sur la valeur therapeutique des trois alcaloides soporifiques (codéine, morphine, narcéine), Thesis, Paris, no. 535, 1877.

6. Pollak, A.: Therap. Monatsh. **7**:545, 1893.

7. von Essen, O.: Therap. Monatsh. **8**:421, 1894.

cases were published by Wolters in 1902,[8] Kyrle in 1912[9] and Dittrich in 1926.[10]

Scheer and Keil[11] wrote about this question in 1934 and reported the seventh case. A woman aged 48 was given 0.065 Gm. of codeine, and an eruption developed on the abdomen, back and thorax; there was a follicular arrangement, with a broad zone of erythema around the individual follicles, the coalescence of which produced a scarlatiniform appearance. The eruption was accompanied by itching. Several days later the patient received a second dose of 0.065 Gm. of the drug, whereupon the eruption spread over the whole body. After forty-eight hours the rash disappeared without any desquamation and the pruritus diminished. Three days later a patch test with codeine phosphate solution was made, which elicited a positive reaction. Patch tests with codeine phosphate, pantopon and opium in powder form and with morphine sulfate solution gave negative results. The authors tried to find antibodies to codeine by the Prausnitz-Küstner and Urbach-Königstein blister methods, but it was found that codeine alone, like morphine, when injected in the skin of normal persons produces wheals artificially. For this reason the aforementioned methods cannot be used to demonstrate antibodies of codeine and morphine. A modified technic, consisting of giving the drug orally to the receivers after giving them an intracutaneous injection of the serum of the patient, caused no general or local eruption. In 1936 Milian[12] stated that eruptions caused by codeine are very rare and found only 7 such cases in the literature.

The main symptoms of this disease are: erythema beginning in a perifollicular form and later developing into a scarlatiniform rash with severe itching. Two other cases have been reported in the United States, by Harris[13] in 1934 and Skorodin[14] in 1935. The second case was that of a student aged 23 who had a scarlatiniform eruption after receiving a small dose of codeine.

Recently I observed a case which can be considered, I think, as the tenth of this series.

REPORT OF A CASE

A workman aged 36 came to the polyclinic on Dec. 14, 1941, complaining of a generalized erythema. It was mainly confined to the abdomen, chest, back and thighs. The patient did not suffer from fever, fatigue or other pathologic sensation.

8. Wolters, M.: Deutsche Praxis **11**:697, 1902.
9. Kyrle, J.: Arch. f. Dermat. u. Syph. **113**:569, 1912.
10. Dittrich, O.: Arch. f. Dermat. u. Syph. **150**:120, 1926.
11. Scheer, M., and Keil, H.: Skin Eruptions of Codeine, J. A. M. A. **102**:908 (March 24) 1934.
12. Milian, G., in Darier, J., and others: Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, vol. 4, p. 751.
13. Harris, M.: Virginia M. Monthly **61**:537, 1934.
14. Skorodin, B.: Illinois M. J. **68**:546, 1935.

According to his statement, the illness started four days previously, before which he had suffered from fits of coughing and received a few pills of codeine, prescribed by his physician. The present disease started with itching followed by the eruption. On December 17 a fading of the eruption was observed. On the following day scaling was noted on the body and palms. I ascertained that on December 9 the patient had received 3 pills of codeine phosphate of 0.015 Gm. each.

Three weeks later, on Jan. 6, 1942, the patient appeared at my request in order to undergo a number of investigations. The skin was normal except for scaling on the palms. I applied patch tests on his arms of codeine powder, codeine solution 1 per cent and morphine solution 1 per cent. On the following day the test sites were normal. At 6 p. m. on the same day I gave the patient 1 pill of codeine phosphate, 0.015 Gm., which he swallowed in my presence. The next day he arrived at 9 a. m. and stated that on the previous evening, some time after taking the codeine, he felt a slight weakness, fatigue, headache and nausea, "as after smoking a lot." At 10:30 p. m. he went to bed. At midnight he felt itching on the whole body, mainly in the armpits. He slept badly and in the morning noticed redness of the whole body. The eruption was a diffuse erythema with no follicular accentuation. The affected parts were mainly the abdomen, thorax, upper part of the thighs, forearms and arms. The patient had no fever, and the pruritns had decreased since the night. He complained of soreness of the throat, and examination revealed redness of the mucosa of the mouth and throat. The blood count showed 7,200 leukocytes, with 42 per cent polymorphonuclear leukocytes, 40 per cent lymphocytes, 3 per cent monocytes and 15 per cent eosinophils.

On the same day, at noon, the patient was presented before the session of the Dermatological Section in Tel-Aviv. At this session Professor Königstein proposed his blister method for search of antibodies, but, instead of injecting a codeine salt in to normal receivers, he proposed giving this drug orally. Unfortunately, the patient refused any further tests. Two days later the eruption disappeared.

In this case, a patient received codeine in small therapeutic doses. A few hours after the ingestion of the drug an erythema developed associated with itching. Contrary to the observations of Dittrich, Scheer and Keil, I did not find any follicular arrangement or accentuation, although I saw the eruption in its first stage. The itching and distribution of the eruption on the skin were similar to those reported by most of the authors. In my case an enanthem was noted. There was eosinophilia in my case, with 15 per cent eosinophils. In 1 of those reported by Dittrich the eosinophil count was 16 per cent. Hypereosinophilia is rather rare in drug eruptions.

SUMMARY

A case is reported of an eruption due to hypersensitivity to codeine. This is the tenth case of the kind to be reported in the literature. The rash appeared a few hours after the ingestion of 0.045 Gm. of codeine phosphate. The second ingestion was followed by the same symptoms. The clinical aspect consisted of erythema, an enanthem, itching and 15 per cent eosinophils, followed some days later by desquamation. Patch tests with codeine, morphine and opium gave negative results.

6, H. Cohen Street.

THE AREA FACTOR IN ROENTGEN IRRADIATION

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It is vaguely known that the size of the exposed area has a distinct influence on the biologic effectiveness of physically measured quantities of radiation. There are occasional references in the literature bearing on this subject, but there is no quotation of any definite numerical ratio of this relationship, especially as regards nonfiltered or slightly filtered radiation. MacComb [1] recently published data showing differences in biologic reaction when areas of various sizes are exposed to nonfiltered roentgen rays of low voltage. However, in a postscript to his article, he stated that his results and conclusions fail to agree with later observations. Meyer [2] published approximate curves showing the effect of variations in area with filtered radiation of high voltage.

In view of the great importance of this area factor in the treatment of cutaneous lesions, it appeared desirable to determine more accurately the effects of variation in area. The quantities of radiation for equal biologic reactions required for various-sized areas were physically determined by us. Since there are no accurately determined experimental data on the effect of variation in area it was necessary to perform many experiments in order to determine the factor responsible for the apparent decrease of effectiveness of radiation with smaller exposed areas.

EXPERIMENTS

The same experimental procedure was followed as that previously described for the study of the effects of variation in radiation intensity on the effectiveness of measured quantities of radiation.[3] It consists of exposing two areas on the

This research was made possible by a grant from the Lillia Babbitt Hyde Foundation.

From the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University.

1. MacComb, W. S.: Low Voltage Roentgen Therapy in Skin Cancer, Am. J. Roentgenol. **41**:437, 1939.

2. Meyer, W.: The Correlation of Physical and Clinical Data in Radiation Therapy, Radiology **32**:23, 1939.

3. MacKee, G. M.; Mutscheller, A., and Cipollaro, A. C.: The Time Factor in Irradiation, Arch. Dermat. & Syph. **47**:490 (April) 1943.

inner surface of the forearm or the thigh of both males and females with various complexions and of different ages. An area 1 inch (2.5 cm.) squared was used as standard.[4] A second area located about ½ inch (1.3 cm.) from the first was exposed to a similar radiation beam and from the same distance. With the use of lead sheet masks the size of the second exposed area on the skin was made either smaller or larger. The exposure time for this area was then made either longer or shorter depending on whether the size of the exposed area was smaller or larger than 1 inch squared. Exposures were made on different persons, with the reactions from previous exposures used as a guide to determine whether an increase or a decrease of exposure time was necessary to obtain final reactions of equal intensities on the two adjoining areas. Observations were made periodically for several weeks. The ratio of the time of exposure or the quantity of radiation applied to each of the two areas was recorded as a measure of the change of effectiveness of radiation caused by a variation in the size of the area exposed. Three series of observations were made, one with 52 kilovolts and no filter, one with 100 kilovolts and no filter and one with 120 kilovolts and a 3 mm. aluminum filter. The results with 52 and 100 kilovolts were found to coincide so well that only two experimental curves were drawn.

During the preliminary plotting of the experimental data it was found that accurate comparison of the intensity of reaction of large and of small areas offered difficulties. With the aid of masks, the size of the fields examined could be made equal, and so any possible influence of optical errors in the comparison of tints of unequal size could be eliminated. However, there still remains the possibility that in a small area recovery or healing may take place at a more rapid rate than in a larger area. To avoid the possibility of any such errors, in addition to the comparison just described, equal areas were compared. Two areas each 5 mm. squared and two areas each 2 mm. squared were exposed. One area of each pair was exposed to nonfiltered radiation and the other area of each pair to filtered radiation (3 mm. of aluminum). Thus more accurate ratios for the points representing small areas were obtained. These points are located on the horizontal portion of the curves.

In measuring the diameter of the tints of the smaller areas it was found that they were invariably smaller than the opening in the lead diaphragm, although the diaphragm was placed near the skin. In addition, the borders of the smaller tinted areas were found to be diffused and shading off toward the edges. This decrease of size of areas and the shading-off were found to be particularly prominent with filtered radiation.

An exact measurement of the size of a tinted area on the skin was found difficult. When 52 and 100 kilovolts of nonfiltered radiation were used, the area of reaction was 1.5 mm. smaller than the mask.

4. As is pointed out later in this article, for nonfiltered or only slightly filtered radiation, the area factor from 2 to 3 cm. squared on upward does not change appreciably. Therefore, 1 inch squared may, for clinical purposes, safely be taken as a "large" area.

This decrease applied to areas of all sizes. With 120 kilovolts and a 3 mm. aluminum filter the area of reaction was 3 mm. smaller than the mask. With further increase in voltage and filtration, it was found that the area of reaction decreased to a greater degree.

The results of the tests made are listed in the accompanying table. Only those exposures are reported in which the reactions show equal cutaneous changes in an area of 1 inch squared and in another adjacent area of a different size. The bronzing which follows the erythema in some cases is also equal if the erythema reactions were equal. But the bronzing following lighter erythemas is often darker than the more intense erythema. This reversal of reaction, however, is not always present, and hence the erythema only is relied on as the indication of reaction.

Experimentally Determined Data Obtained with Radiations of Two Different Qualities on Cutaneous Areas of Various Sizes

No.	Kilovolts	Area I	Area II	Exposure Area I	Exposure Area II
97	100, no filt.	2.5 cm.	10 cm.	330 r	300 r
99	100, no filt.	2.5 cm.	4.5 cm.	330 r	320 r
	100, no filt.	2.5 cm.	2.5 cm.	330 r	330 r
86	52, no filt.	2.5 cm.	1 cm.	330 r	355 r
89	100, no filt.	2.5 cm.	5 mm.	330 r	440 r
94	52, no filt.	2.5 cm.	2 mm.	330 r	1,000 r
115	120, 3 mm. Al.	2.5 cm.	9 cm.	540 r	480 r
114	120, 3 mm. Al.	2.5 cm.	4.5 cm.	540 r	500 r
	120, 3 mm. Al.	2.5 cm.	2.5 cm.	540 r	540 r
111	120, 3 mm. Al.	2.5 cm.	1 cm.	540 r	700 r
110	120, 3 mm. Al.	2.5 cm.	5 mm.	540 r	1,100 r
128	52, no filt.	5 mm.	.....	440 r	.....
	120, 3 mm. Al.	.....	5 mm.	.....	1,040 r

For the tests with nonfiltered radiation, a total of 18 persons were exposed. In only 6 did the tints match, and these data are plotted in the curve marked "nonfiltered." For the tests with filtered radiation, 17 persons were exposed. Equal tints were obtained in 5, and these data are plotted in the curve marked "3 mm. aluminum." For highly filtered radiation, i. e. 180 to 200 kilovolts and 0.5 to 0.7 mm. copper filter, the data published by Meyer are plotted in the curve marked "hard rays strongly filtered."

On the vertical axis of chart 1 the diameter of the exposed areas are indicated, and on the horizontal axis the total roentgens applied as single doses are indicated. Thus the points represent the total roentgens required to obtain with various-sized areas identical reactions as with 330 for nonfiltered or with 540 filtered through 3 mm. of aluminum and on an area of 2.5 cm. squared.

With nonfiltered or lightly filtered radiation, the effect of variation in area is slight in areas larger than 2 cm. squared. In other words, in order to obtain equal biologic reactions in areas larger than 2 cm.

squared, no changes are necessary, but for areas smaller than 2 cm. squared, considerably increased quantities of radiation are required. For highly filtered radiation of high voltage the effect of variations in area is slight in areas larger than 10 cm. squared. For equal biologic reactions in areas smaller than 10 cm. squared, increased quantities in radiation are required. A glance at the curves in chart 1 demonstrates the exact relation between various areas and the number of roentgens required for equal biologic reactions.

It has been found that the effectively irradiated areas are smaller than the opening in the diaphragm through which the roentgen rays

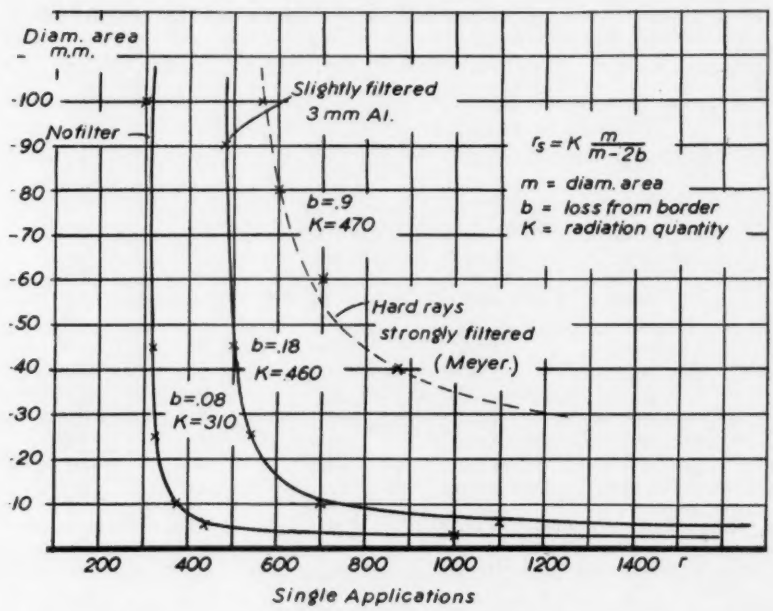

Chart 1.—The roentgens required to obtain with various-sized areas identical reactions with nonfiltered, lightly filtered and heavily filtered radiation.

pass. In order to be certain that a small lesion is effectively irradiated over its entire extent, it should be shielded with an opening that is larger than the lesion all around the periphery by an amount previously stated. Therefore, the ratios for roentgens required between larger and smaller areas is not the same for all qualities of radiation, but it increases substantially with filtration.

One exception may develop out of conditions often present in clinical therapeutic irradiation. The lead diaphragm used may emit from its border considerable quantities of secondary radiation, especially if the voltage applied to the x-ray tube is distinctly above the characteristic

alpha K line of lead, i. e., above 87.2 kilovolts.[5] In clinical irradiation the formation of these secondary rays should be avoided either with secondary filters between the diaphragm and the patient or by suitable spacing. Thus the considerations herein are exclusive of diaphragm radiation.

COMMENT

The similarity in shape of the curves resulting from variation in area with those reported earlier from variation in intensity [3] suggests at once a similarity of the effects from varying the exposed area and that from varying the intensity of radiation. The quantity of secondary radiation formed is clearly a function of the exposed volume, and thereby this problem involves geometric relations which control the quantity of secondary radiation formed in the tissues and in particular those secondary rays that reach back to the skin and produce the visible erythema. The following geometric consideration may be applied.

In chart 2 *A* let us assume that the radiation coming from the anode of the x-ray tube passes through the opening in a lead diaphragm placed near the skin. We also assume that this diaphragm emits no secondary rays and that it has a square or circular opening. The volume of tissue of which A-O_1-O_2-B is a cross section is exposed. In this exposed volume the atoms struck by photons emit secondary radiation which, according to the wavelength or the kilovoltage applied to the x-ray tube, travels the distance b in the tissues.

Owing to the fact that from zone *b* secondary radiation is sent out into zone *c*, from which no secondary radiation is returned back to zone *b*, there is a gradual fading-off of the total radiation intensity from zone *a*, which has the maximum intensity through the gradually fading-off zone *b* to the faint zone *c*. In similar fashion, there is a decrease in zone *f* near the skin except that all the secondary radiation passing through the skin is lost into the air.

In the small corner zones *g*, which result from the overlapping of zones *b* and *f*, there is therefore a considerable decrease of secondary radiation, and consequently the tissues in that zone and the skin receive substantially less radiation than the central area directly above the volume *a*. The decrease of intensity of the exposed area accounts for a substantial loss of secondary radiation at the border of the irradiated field. Accordingly, this decrease of the size of the effectively irradiated field should depend on the wavelength of the primary beam which determines the distance of travel of the secondary radiation. On this basis this hypothesis is being tested and verified in the experiments that follow:

The skin area O_1-O_2 is irradiated through the opening in the lead diaphragm which has a diameter m. The effectively irradiated area

5. Siegbahn, M.: Spektroskopie der Roentgenstrahlen, ed. 2, Berlin, Julius Springer, 1931.

which shows an erythema reaction is m — 2b. Hence, for a very large area irradiated, the radiation quantity r_s approaches K, which is the radiation quantity required for an erythema when a large field is exposed. For smaller areas, a larger number of roentgens are required for the same biologic effect. Hence the biologic effectiveness of the applied radiation decreases as $\frac{m}{m-2b}$. In order to obtain equal biologic changes for diaphragm openings (m) of various sizes the quantity of radiation (r_s) required may be calculated thus: $r_s = K\frac{m-2b}{m}$. This condition should hold so long as m is greater than 2b.

In figure 1 the curves drawn were calculated with this equation. By the trial method it was found that the constants which made this

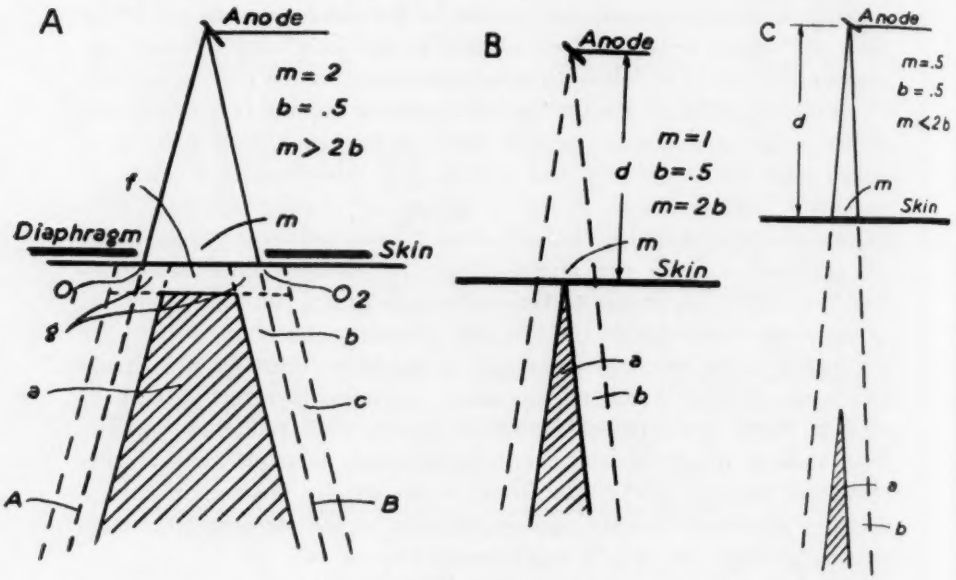

Chart 2.—*A* illustrates a geometric explanation for the gradual fading of the radiation effect at the borders when a large area is exposed. *B*, fading of the radiation effect at the border when a small area is exposed. *C*, recession of the full intensity area into the depth of the tissue when very small areas are exposed.

equation fit the experimental data, as plotted in chart 1, are the following:

52 and 100 kv.	No filter	$K = 310$ $b = 0.08$	Experim. $b = 0.075$
120 kv.	3 mm. Al filter	$K = 460$ $b = 0.18$	Experim. $b = 0.15$
180-200 kv.	0.5-0.75 mm. copper filter (Meyer)	$K = 470$ $b = 0.9$	not observed

It may be pointed out that the decrease in the areas of erythema as measured on patients and the values of b which were theoretically found agree closely. This would indicate the correctness of the assump-

tions that secondary radiations from the irradiated zone are lost into the adjacent unexposed tissues. The value given to K may be varied according to the reaction desired and the quality of the radiation used. Thus the intensity of the erythema in the cases quoted obtained with high voltage and heavily filtered radiation is less than that of the non-filtered or only slightly filtered beams.

There still remains to be considered the case when m equals 2b (chart *2 B*). The area of full intensity (*a*) is triangular, and the point of the triangle is at the surface of the skin. If, however, m is smaller than 2b (chart *2 C*), the point of the triangle recedes to the depth, and thus the geometric relations are such that

$$r_a = K\left(\frac{m}{2db-d}\right)^2 \text{ or } K\left(\frac{m}{d\,(2b-1)}\right)^2.$$

These conditions represent a possibility of a method of relatively decreasing the erythema effect on the skin while causing in the depth a volume of considerably increased intensity. On the contrary, if a small lesion, e. g. a wart or a small epithelioma, is to be treated through a

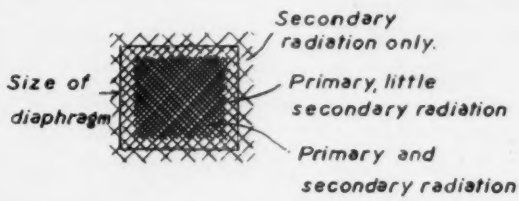

Chart 3.—The effect of loss of radiation from the exposed areas into the adjacent nonexposed tissues.

small diaphragm it should be exposed to nonfiltered or only slightly filtered radiation. Radiation of high voltage and heavily filtered radiation applied through small openings would give rise to the intensified triangle in the depth and also to a much reduced effectiveness of the radiation at or near the surface of the skin. This problem is still under investigation and is to be reported on at a later date.

SUMMARY AND CONCLUSIONS

The measured roentgens required to produce equal visible changes in the skin for various sizes of exposed areas with different degrees of filtration were experimentally determined and are presented herein.

The areas of the erythema reaction are found to be smaller than the exposed areas, particularly with highly filtered radiation.

Measured and theoretically calculated values for the decrements in reaction area are given.

It is shown that the variation in area with nonfiltered or slightly filtered radiation is slight with areas above 2 cm. squared; it is also slight with highly filtered radiation when areas above 10 cm. are exposed.

In order to include all parts of a small lesion, it is necessary to increase the diameter of the exposed field at least by 1.5 mm. for unfiltered and 3 mm. for slightly filtered radiation.

The assumption is made that secondary radiation sent from the exposed tissues to adjoining nonexposed tissues causes a shading-off of intensity near the border and the surface of the exposed volume of tissue.

The equation derived from these assumptions is tested and found over a stated range to fit the experimentally determined values.

Agreement of the curves with calculated values and close agreement of measured decrements in area of erythema with those calculated are presented in support of the correctness of the assumptions made.

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MAPHARSEN AND NEOARSPHENAMINE ADMINISTERED BY CONTINUOUS INTRAVENOUS DRIP METHOD

TOXICITY FOR RABBITS

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As previously reported,[1] we have observed that five daily doses of neoarsphenamine varying from 0.001 to 0.008 Gm. (totaling 0.005 to 0.04 Gm.) and five daily doses of mapharsen varying from 0.0005 to 0.004 Gm. (totaling 0.0025 to 0.02 Gm.) per kilogram of body weight administered by the intravenous drip method were well tolerated by rabbits. The minimal curative doses in the treatment of acute testicular syphilis of these animals were found to be approximately 0.004 Gm. of neoarsphenamine and 0.001 Gm. of mapharsen administered once a day for five days in succession, totaling 0.02 Gm. of neoarsphenamine and 0.005 Gm. of mapharsen per kilogram of body weight.

The purpose of the present investigation was to determine the toxicity of neoarsphenamine and mapharsen administered by the intravenous drip method to normal rabbits as compared with their toxicity when given by syringe in single doses at a rate of injection usually employed for determining the maximum tolerated doses of the organic arsenical compounds for the lower animals.

EXPERIMENTAL PROCEDURE

The mapharsen employed was the pure compound, supplied by Parke, Davis & Co., Detroit, in order that accurate dosage per kilogram of weight might be obtained. Solutions were prepared in 5 per cent solutions of dextrose and neutralized before administration. With the intravenous drip method of administration each dose was prepared in 80 cc. of dextrose solution and administered intravenously at the rate of 15 to 30 drops per minute for a period of three hours and fifty-three minutes to four hours. Five doses varying from 0.004 to 0.02 Gm. per kilogram of weight were given at daily intervals (table 1). Each dose of neoarsphenamine was also administered in 80 cc. of a 5 per cent solution of dex-

From the Research Institute of Cutaneous Medicine.

1. Kolmer, J. A., and Rule, A. M.: Massive Arsenotherapy by the Continuous Intravenous Drip Method in the Treatment of Acute Syphilis of Rabbits, Arch. Dermat. & Syph. **44**:1055 (Dec.) 1941.

trose at the same rate of injection. Five doses varying from 0.05 to 0.15 Gm. per kilogram of weight were injected at daily intervals (table 1). Two rabbits were treated with each dose of the two compounds.

TABLE 1.—*Toxicity of Neoarsphenamine and Mapharsen Administered Daily to Rabbits for Five Days in Succession by the Intravenous Drip Method* *

Compounds	Dose, Gm. per Kg.	Number Doses	Total Dosage, Gm. per Kg.	Results
Neoarsphenamine	0.050	5	0.250	Lived indefinitely
	0.050	5	0.250	Lived indefinitely
	0.060	5	0.300	Lived indefinitely
	0.060*	5	0.300	Lived indefinitely
	0.080	3	0.240	Died after third dose
	0.080	3	0.240	Died after third dose
	0.100	2	0.200	Died after second dose
	0.100	3	0.300	Died after third dose
	0.150	1	0.150	Died after first dose
	0.150	1	0.150	Died after first dose
Mapharsen	0.004	5	0.020	Lived indefinitely
	0.004	5	0.020	Lived indefinitely
	0.008	5	0.040	Lived indefinitely
	0.008	5	0.040	Lived indefinitely
	0.012	5	0.060	Lived indefinitely
	0.012	5	0.060	Died twenty-nine hours after fifth dose
	0.015	4	0.060	Died after fourth dose
	0.015	3	0.045	Died after third dose
	0.020	2	0.040	Died after second dose
	0.020	1	0.020	Died after first dose

* Time required for administration of each dose: three hours and fifty-three minutes to four hours. Each compound administered in 5 per cent solution of dextrose.

TABLE 2.—*Toxicity of Single Doses of Neoarsphenamine and Mapharsen Administered Intravenously to Rabbits by Syringe* *

Compounds	Dose, Gm. per Kg.	Results
Neoarsphenamine	0.150	Lived indefinitely
	0.150	Lived indefinitely
	0.200	Lived indefinitely
	0.200	Lived indefinitely
	0.225	Lived indefinitely
	0.225	Died in five days
	0.250	Died in one day
	0.250	Died in eighteen hours
	0.300	Died in less than four hours
	0.300	Died in less than four hours
Mapharsen	0.004	Lived indefinitely
	0.004	Lived indefinitely
	0.010	Lived indefinitely
	0.010	Lived indefinitely
	0.015	Lived indefinitely
	0.015	Lived indefinitely
	0.020	Died in twenty-four hours
	0.020	Died in thirty-six hours
	0.030	Died in two hours
	0.030	Died in two hours

* Compounds administered in 5 per cent solution of dextrose at the rate of twelve to fifteen seconds per one-tenth cubic centimeter.

By the syringe method of administration mapharsen was employed in 0.25 per cent and neoarsphenamine in 1 per cent solutions in 5 per cent solution of dextrose. Each solution was injected at the rate of 0.1 cc. per twelve to fifteen seconds. The doses of mapharsen varied from 0.004 to 0.03 Gm. and those of neoarsphenamine from 0.150 to 0.300 Gm. per kilogram of body weight (table 2). Single

doses of each compound were administered, 2 rabbits being likewise used for each dose of the two compounds.

All surviving animals were kept under observation for ten days after treatment, at the end of which time they were killed for microscopic examination of the kidneys, liver, spleen, lungs, cerebrum and meninges for possible histologic evidences of injury. The same organs were also examined in the case of all animals succumbing before the expiration of this period.

RESULTS

Toxicity by the Intravenous Drip Method of Administration.—As shown in table 1, the maximum tolerated dose of mapharsen was approximately 0.012 Gm. per kilogram of body weight administered once daily for five days in succession and totaling 0.06 Gm. per kilogram. This dose, therefore, was similar to that reported by Magnuson, Raulston and Muff [2] in the case of dogs, which showed a maximum tolerated dose of about 0.01 Gm. per kilogram of weight when given in five daily doses by the intravenous drip method of administration.

Microscopic examination of the meninges, cerebrum, kidneys, lungs, liver and spleen of animals killed ten days after the fifth injection of 0.004 and 0.008 Gm. per kilogram showed no evidences of injury. Examination of those animals succumbing after the administration of 0.012 to 0.02 Gm. per kilogram showed histologic changes quite similar to those observed by Kolmer and Lucke [3] after the administration to rabbits of eight to ten injections of disodium arsphenamine in doses of 0.01 Gm. per kilogram of weight. The meninges usually showed slight hyperemia with minute areas of focal hemorrhages in the cerebrum, some passive congestion and diffuse capillary edema of the lungs, slight periportal fibrosis with small areas of focal necrosis of the peripheral portions of the lobules of the liver, congestion with degenerative changes in the convoluted tubules of the kidneys and congestion of the spleen. It is significant that no changes in these organs were observed after five doses of 0.004 Gm. each per kilogram of weight, which corresponds to a dose of 0.02 Gm. per kilogram, or a total of 1.2 Gm. per 60 Kg., ordinarily administered to adult human beings in the massive arsenotherapy of early syphilis with this compound. Nevertheless, histologic injuries may be produced in syphilitic human beings, with special reference to hemorrhagic encephalopathy, even though not observed in normal rabbits.

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2. Magnuson, H. J.; Raulston, B. O., and Muff, A.: The Toxic Dose of Mapharsen Given by the Continuous Drip Method, Ven. Dis. Inform. **22**:157, 1941.

3. Kolmer, J. A., and Lucke, B.: A Study of the Histologic Changes Produced Experimentally in Rabbits by Arsphenamin, Arch. Dermat. & Syph. **3**:483 (April, pt. 2) 1921.

As shown in table 1, the maximum tolerated dose of neoarsphenamine was approximately 0.06 Gm. per kilogram of body weight administered once daily for five days in succession and totaling 0.3 Gm. per kilogram. Under the circumstances the maximum tolerated dose by this route of administration was about five times higher than that of mapharsen.

Microscopic examination of the meninges, cerebrum, kidneys, lungs, liver and spleen of animals killed ten days after the five injections of 0.05 and 0.06 Gm. per kilogram, however, showed histologic evidences of injury similar to those observed by Kolmer and Lucke [4] after the administration to rabbits of three to ten injections of neoarsphenamine in doses of 0.02 Gm. per kilogram of weight, even though they survived with no clinical evidences of toxicity.

These changes were particularly pronounced in the kidneys, which showed varying degrees of rather severe tubular nephritis (especially of the convoluted tubules) due to the fact that neoarsphenamine is particularly renotoxic. Tubular nephritis was also observed in those rabbits succumbing after two to three doses of 0.08 and 0.1 Gm. per kilogram, although of lesser degree owing to short survival. In this connection it is to be remembered, however, that the five doses of 0.05 Gm. each at daily intervals totaled 0.25 Gm. per kilogram, which is equivalent to 15 Gm. per 60 Kg. Under the circumstances the total of 4 to 5 Gm. given adults in the massive arsenotherapy of early syphilis may be relatively safe although apparently more likely to injure the kidneys than a total dosage of 1.2 Gm. of mapharsen.

Otherwise, the histologic injuries observed after multiple injections of neoarsphenamine in doses ranging from 0.05 to 0.1 Gm. per kilogram consisted of slight hyperemia of the meninges with occasional small hemorrhagic intravasations but no focal hemorrhages in the cerebrum, congestion of the lungs and spleen and numerous small areas of lobular necrosis of the liver. The 2 animals succumbing in less than twenty-four hours after one dose of 0.15 Gm. per kilogram, due to the fact that rabbits have a lower tolerance for arsphenamine and neoarsphenamine than rats and mice, showed nothing more definite than acute congestion with thrombi of agglutinated erythrocytes in the organs examined.

Toxicity of Single Doses Administered Intravenously by Syringe.—As shown in table 2, the maximum single tolerated dose of mapharsen administered by syringe to rabbits was approximately 0.015 Gm. and of neoarsphenamine approximately 0.225 Gm. per kilogram of weight.

4. Kolmer, J. A., and Lucke, B.: A Study of the Histologic Changes Produced Experimentally in Rabbits by Neo-Arsphenamin, Arch. Dermat. & Syph. **3**:515 (April, pt. 2) 1921.

It will be observed, therefore, that the tolerance of rabbits for mapharsen was three to four times higher by the intravenous drip method of administration (maximum tolerated dose 0.04 to 0.06 Gm.) than by the syringe injection of single doses (maximum tolerated dose 0.015 Gm.). The same was true but to a much lesser degree in the case of neoarsphenamine, the maximum tolerated dose by the drip method being approximately 0.300 Gm. and by the syringe method approximately 0.225 Gm. per kilogram of weight. In other words, the results were further evidence of the relation of speed injection ("speed shock") to toxicity, as described by Hirshfeld, Hyman and Wanger.[5]

Furthermore, while we could discover no histologic evidences of injury in the organs of rabbits killed ten days after five intravenous injections of mapharsen by the drip method totaling 0.02 and 0.04 Gm. per kilogram, the kidneys of rabbits killed ten days after the intravenous injection of 0.015 Gm. per kilogram showed tubular nephritis with slight congestion of the lungs and spleen along with slight coagulation necrosis of the liver, the changes being similar to those observed by Kolmer and Lucke [3] after the administration to rabbits of single doses of 0.08 Gm. of disodium arsphenamine. Nephritis was also observed in the animals succumbing in twenty-four to thirty-six hours after the intravenous injection of 0.02 Gm. of mapharsen per kilogram, but to a lesser degree because of the short survival. In these 2 animals, as well as in those succumbing in two hours after the injection of 0.03 Gm. per kilogram, the histologic changes were only those of acute congestion in the organs examined.

Histologic examination of the organs of rabbits killed ten days after the administration of 0.15 to 0.225 Gm. of neoarsphenamine per kilogram of weight showed severe tubular nephritis, congestion of the meninges with occasional small hemorrhagic extravasations, congestion of the lungs, congestion of the spleen with slight necrosis and numerous small areas of irregularly distributed necrosis of the lobules of the liver, exactly similar to the changes observed by Kolmer and Lucke [4] following the administration of 0.2 Gm. per kilogram of weight to rabbits. The changes observed in the animals succumbing in four to twenty-four hours after the administration of 0.25 to 0.3 Gm. were slight, essentially only acute congestion in the organs examined, because of the short survival.

SUMMARY

1. The maximum tolerated dose of mapharsen for rabbits with the continuous intravenous drip method of administration was about 0.012 Gm. per kilogram of weight once a day for five days in succession,

5. Hirshfeld, S.; Hyman, H. T., and Wanger, J. J.: Influence of Velocity on Response to Intravenous Injections, Arch. Int. Med. **47**:259 (Feb.) 1931.

totaling 0.06 Gm. per kilogram. With the syringe method of administration the single maximum tolerated dose was about 0.015 Gm. per kilogram.

2. The maximum tolerated dose of neoarsphenamine for rabbits with the continuous intravenous drip method of administration was about 0.06 Gm. per kilogram of weight once a day for five days in succession, totaling 0.3 Gm. per kilogram. With the syringe method of administration the single maximum tolerated dose was about 0.225 Gm. per kilogram.

3. Under the circumstances the tolerance of rabbits for both compounds was better with the continuous intravenous drip method of administration of five doses at daily intervals than with the administration of single doses by syringe injection; this was particularly true in the case of mapharsen.

4. No histologic evidences of injury in the meninges, cerebrum, liver, kidneys, lungs and spleen were observed after five intravenous injections of mapharsen in doses of 0.004 and 0.008 Gm. per kilogram at daily intervals by the intravenous drip method of administration, the former totaling 0.02 Gm. per kilogram and equivalent to 1.2 Gm. per 60 Kg. ordinarily employed in the massive arsenotherapy of human beings with early syphilis. Single doses of 0.015 Gm. per kilogram, however, produced tubular nephritis with histologic changes in the lungs, spleen and liver.

5. Tubular nephritis of varying severity, as well as histologic evidences of injury of the meninges, cerebrum, liver, kidneys, spleen and lungs, was observed after five daily doses of 0.05 Gm. of neoarsphenamine, totaling 0.25 Gm. per kilogram and equivalent to 15 Gm. per 60 Kg. This total dosage, however, was about four times higher than that given in the massive arsenotherapy of human beings with early syphilis. Severe tubular nephritis, along with histologic evidences of injury of other organs, was also observed after the intravenous injection of single doses of 0.15 Gm. or larger amounts per kilogram of weight.

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USE OF DIETHYLSTILBESTROL IN TREATMENT OF KRAUROSIS VULVAE

PRELIMINARY REPORT

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Kraurosis vulvae is a rare disease occurring about the time of the menopause or later. It is characterized by intense itching of the vulva and various stages of inflammation and leukoplakia of the labia minora, clitoris and vaginal orifice. The diseased tissue is brittle and consequently fissures readily. These fissures are tender and painful. The subsequent course of kraurosis vulvae is that of atrophy, leukokeratosis and eventually epitheliomatosis.

Kraurosis vulvae is chronic, is unresponsive to topical treatment and leads to serious complications. Cole stated the belief that kraurosis vulvae always eventuates in cancer if it continues sufficiently long. To date surgical intervention has been considered the best form of therapy. However, to be effective vulvectomy must be extensive, with subsequent loss of (sexual) function and disfigurement. Although injections of alcohol or sclerosing fluids may produce good results, the relief is temporary, and there is always the danger of sloughing. Roentgen treatment is usually effective, but with this also the relief is temporary. According to MacKee,[1] "It is advisable to discontinue x-ray treatment, if the pruritus is not relieved as a result of three or four fractional treatments."

The therapeutic results with estrogenic substances to date, as reported in the literature and from practical experiences, have been uncertain. Diethylstilbestrol has been used successfully in the treatment of menopausal symptoms when estrogenic substances have failed. This success is noted particularly in the use of oral and topical preparations of the drug. Wharton[2] used diethylstilbestrol for postmenopausal pruritus vulvae and found that the "benefit was definite and sometimes remarkable."

The purpose of this communication is to describe a simple, practical and successful treatment that was used in 2 cases of kraurosis

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From the Radiotherapy Department of Montefiore Hospital.

1. MacKee, G. M.: X-Ray and Radium in the Treatment of Diseases of the Skin, ed. 3, Philadelphia, Lea & Febiger, 1938.

2. Wharton, L.: Treatment of Pruritus of Perineum, Labia and Vagina by Newer Methods, South. M. J. **34**:694-698 (July) 1941.

vulvae. Two patients responded favorably to the topical application of diethylstilbestrol in the form of suppository and ointment after other methods of treatment ordinarily used for this disease, including partial vulvectomy, failed to give relief.

REPORT OF CASES

CASE 1.—M. L., aged 60, a Jewish housewife, was first seen on Sept. 23, 1940 in the radiotherapy department, to which she was referred for the treatment of severe vulvar pruritus. The symptom had been present for ten years and had become progressively worse.

Her gynecologic history was essentially irrelevant. She had three children, and all of her pregnancies terminated uneventfully. The menopause occurred twelve years previously, at the age of 48. There were no unusual climacteric symptoms.

For the relief of the severe pruritus of the vulva, she used many topical preparations, with only temporary effect. In 1938 the patient was given estrogenic substances both by inunction and by injection. This treatment was continued for three months without improvement. In November 1939 a partial vulvectomy was performed. The tissue was examined, and the histologic diagnosis confirmed the clinical diagnosis of kraurosis vulvae. After the operation there were no symptoms for six months. Then itching about the genitals recurred and spread to the perianal area. It was more severe than ever before. She was referred to the radiotherapy department in September 1940.

The patient was well developed and well nourished. Examination of the ears, nose and throat showed no abnormalities. There was no adenopathy. The thyroid gland was normal. The heart, lungs and abdomen were essentially normal. Vaginal examination revealed evidence of a partial vulvectomy; the labia minora were absent, and the labia majora were about half the normal size. The skin and mucous membrane of the labia, the perineum and the perianal area were dry, thickened, lichenified and excoriated. The introitus was fissured and dry, and superficial erosions were present at the lower angle blending with areas of leukoplakia at the lateral margins. The vaginal wall was slightly thickened, dry and of whitish color. The cervix was small, and the uterus was not palpable. The fornices were clear. Rectal examination revealed excoriations of the perianal area. The skin was dry and erythematous. There were two small hemorrhoidal tags. Digital examination of the rectum showed nothing abnormal. The extremities were normal. A complete blood count and the urine were normal, and the Wassermann reaction of the blood was negative. She received a series of eight low voltage unfiltered roentgen ray treatments. Each treatment consisted of 100 r, and treatments were given at weekly intervals. After this she remained symptom free for six months. When the symptoms recurred, the patient was treated with 4 per cent estrone (theelin) ointment without any beneficial effects. An additional series of seven treatments with roentgen rays failed to cause improvement. It was then decided to use diethylstilbestrol.

Diethylstilbestrol was used in the form of vaginal suppositories, each containing 0.5 mg. The patient was instructed to use one suppository morning and evening. After two weeks there was decided improvement in the subjective and

objective symptoms. The patient was then instructed to use one suppository daily, which she has done up to the present. There have been no symptoms and no cutaneous or mucous membrane lesions for over one year. There were no untoward symptoms from the use of the drug.

CASE 2.—S. C., aged 65, a Jewish housewife, was seen in private practice in January 1942, complaining of pruritus of the vulva. This symptom had been present for the past three years and had become progressively worse during the last six months.

The past history was essentially irrelevant. The menstrual periods were regular. There was moderate dysmenorrhea before her pregnancies but none thereafter. The patient had been pregnant three times; all three children were born at full term and were living and well. The menopause had occurred fifteen years previously, at the age of 50. The patient had occasional flushes but no other climacteric symptoms. There was no vaginal discharge.

Previous treatment of the pruritus consisted of application of topical ointments and injection of an estrogen (exact dose not known). However, the patient was not relieved of her symptoms.

The patient was well developed and well nourished. Dental caries was present. The nose, ears and throat were essentially normal. There was no adenopathy. The thyroid gland was normal. The heart, lungs and abdomen were essentially normal. Vaginal examination revealed extreme dryness of the cutaneous and mucous surfaces of the labia majora. The tissue was lichenified and covered with numerous excoriations and deep fissures. The labia minora were thickened, deeply fissured and leukokeratotic. The vaginal wall was moderately dry and slightly whitish. The external os of the cervix was eroded and had a deep fissure on the left side. The parametria were clear. The uterus was not palpable. Rectal examination revealed a few scattered excoriations on the perineum. Digital examination revealed no abnormalities. The results of urinalysis and of a complete blood count were normal, and the Wassermann reaction of the blood was negative.

Fifty per cent silver nitrate solution was applied to the cervix. Two per cent silver nitrate solution was applied to the fissures on the labia. Vaginal suppositories each containing 0.5 mg. of diethylstilbestrol were used twice daily. Four per cent diethylstilbestrol in zinc oxide ointment was applied to the vulva three times a day.

Within a week the patient felt much better, the itching subsided, the fissured areas were no longer painful and she was able to sleep. The vulva appeared less irritated; the fissures were shallow, and the mucosa was soft and pliable.

After the patient had been on this regimen for three weeks, she decided to discontinue the treatment, since she felt so greatly improved. However, the pruritus began to recur within about one week. The patient then resumed treatment with the diethylstilbestrol suppositories and ointment. The symptoms have been controlled, and there has been continuous improvement in the appearance of the skin and mucous membrane of the vulva. The patient has continued to use the suppositories up to the present. There were no apparent ill effects from the use of diethylstilbestrol.

SUMMARY

Two patients with kraurosis vulvae were treated with diethylstilbesterol in the form of an ointment and vaginal suppositories. There was improvement of subjective and objective symptoms after other methods of treatment had failed. The skin and mucous membrane assumed an almost normal appearance and remained so while under treatment. Obviously further studies on a larger series of cases are required before the true evaluation of this drug in the treatment of kraurosis vulvae can be ascertained.

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BRONCHIAL ASTHMA FOLLOWING THE INHALATION OF POWDERED NEOARSPHENAMINE

ATTEMPTED ORAL HYPOSENSITIZATION

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The toxic effects and anaphylactic reactions from the intravenous injection of the arsphenamines in the treatment of syphilis are well known. The reactions may manifest themselves in various forms, but rarely is the upper part of the respiratory tract involved as in an attack of asthma.

De Beyrouth [1] reported a reaction in a syphilitic patient, aged 38, without a previous history of asthma. During the third injection of 0.75 Gm. of neoarsphenamine the patient experienced an attack of asthma, which disappeared when the injection was stopped. The next attack followed the injection of 0.45 Gm. and lasted four days. As little as 0.05 Gm. of neoarsphenamine produced a reaction. Treatment was entirely discontinued after a violent attack occurred in the course of the administration of 0.3 Gm. of neoarsphenamine.

Of even less frequent occurrence are anaphylactic reactions from local contact with the drug or from its inhalation. Klauder [2] reported a reaction in a physician with a chronic dermatitis of the hands which lasted for eight months. The sensitivity was proved by avoidance and reexposure to arsphenamine and neoarsphenamine. On opening an ampule of neoarsphenamine for dissolution he sneezed, coughed and was conscious of a sense of pressure and constriction in the chest. At other times he had definite attacks of asthma. When he wore rubber gloves and administered arsphenamines prepared by others, he was free from asthmatic symptoms and from dermatitis. A subcutaneous injection of 1 drop of a 1 to 100 to 1 to 1,000 dilution of arsphenamine caused a local reaction lasting for months. Oral desensitization was attempted but was discontinued because of persistent symptoms at the site of positive reactions to previous scratch tests with 2 per cent arsphenamine. The patient was advised to avoid inhalation of and contact with arsphen-

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1. De Beyrouth, M.: Note sur un cas d'asthme provoqué par des injections denéo-salvarsan, à intensité variable suivant des doses injectés, Bull. Soc. franç. de dermat. et syph. **31**:203-205, 1920.

2. Klauder, J. V.: Hypersensitiveness to Local Contact with the Arsphenamins Producing Chronic Eczematoid Dermatitis and Asthmatic Symptoms, Arch. Dermat. & Syph. **5**:486-492 (April) 1922.

amines. During a subsequent period of one year's observation he had no further symptoms, although he continued to administer arsphenamine daily. Although it was not definitely stated by the author, it is assumed that the patient did not have asthmatic attacks during the attempted oral desensitization.

Vuletic [3] in 1933 reported that both he and his technician had had recurrent episodes of sneezing and several attacks of asthma after coming in contact with arsphenamine. This reaction occurred in a health station in which there was considerable dust, but they were symptom free when exposed to the drug in other localities. Neither of these subjects gave a personal or a familial history of other allergic manifestations.

Szarvas [4] in 1934 reported the occurrence of asthmatic attacks and dyshidrosis, or dermatitis, on the left hand from contact with arsphenamine. After avoidance for five or six years, reexposure to the drug precipitated a recurrence of the asthma. Later he gave himself an intravenous injection of arsphenamine and did not experience any asthma. There is no substantial evidence of frank sensitivity to arsphenamine in this case, as the inhalation of the drug was reported to cause asthma but there was no reaction when it was taken intravenously. The patient apparently was nonsyphilitic.

In 1936 Cerri [5] reported a case of asthma as an unusual sensitization to arsphenamine in powdered form.

J. E. Moore [6] reported the occurrence of asthma and urticaria in a pharmacist following the inhalation of tryparsamide. In his textbook "Modern Clinical Syphilology" Stokes [7] mentioned this case in addition to the case of Klauder's. Both authors considered asthma from arsphenamine as rare. Ormsby,[8] in his book "A Practical Treatise on Diseases of the Skin," did not mention asthma in his list of reactions due to arsphenamine.

Further substantiation of the rarity of asthma as a manifestation of sensitivity to arsphenamine is clearly indicated in the work of Cole and

3. Vuletic, A.: Ueber Salvarsanüberempfindlichkeit und akute Salvarsanintoxikation infolge beruflicher Benetzungen der Finger mit Salvarsanlösungen, Arch. f. Dermat u. Syph. **169**:436-441, 1933.

4. Szarvas, A.: Ueber die durch Arsenobenzolpräparate hervorgerufenen asthmatischen, Anfälle und Dyshidrose, Deutsche med. Wchnschr. **60**:1751-1752 (Nov. 16) 1934.

5. Cerri, B.: Sopra un caso non comune di sensibilizzazione all'arsenobenzolo in polvere, Gior. med. d. Alto Adige **8**:635-641 (Nov.) 1936.

6. Moore, J. E.: The Modern Treatment of Syphilis, ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1941, p. 102.

7. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1926.

8. Ormsby, O. S.: A Practical Treatise on Diseases of the Skin, ed. 5, Philadelphia, Lea & Febiger, 1937.

his associates.[9] In a review of the cases of 1,212 patients receiving 78,340 injections of arsphenamines—arsphenamine, neoarsphenamine, sulfarsphenamine and tryparsamide—asthma was not mentioned as a reaction.

Strickler, Munson, Sidlich and Strauss [10] reported the reactions to the intravenous administration of arsphenamine observed in nonsyphilitic persons. They gave each of 114 nonsyphilitic persons a single injection of arsphenamine. Reactions were headache, chills, fever, nausea, vomiting, diarrhea and backache, and dermatitis. Syphilitic patients gave like reactions. There was no mention of asthma.

Cole and others [11] reported arsenical reactions in the treatment of syphilis. Of 75,000 patients treated for syphilis 8,810 patients receiving 117,360 injections of arsenicals had reactions. Asthma was not mentioned as an arsenical reaction in this discussion.

Phelps and Washburn [12] described the toxic effects of arsenical compounds used in the treatment of syphilis in the United States Navy and gave the results from 272,354 injected doses of neoarsphenamine and other compounds of arsenic. Asthma was not mentioned as an arsenical reaction.

Following is a report of a case of bronchial asthma following the inhalation of powdered neoarsphenamine in which an attempt at oral hyposensitization was made.

REPORT OF A CASE

A white physician was first seen in the clinic in January 1939, complaining of multiple manifestations of allergy.

History.—During the winter of 1929-1930 he had recurrent nasal obstruction and a postnasal drip, which was diagnosed as acute cold and sinus trouble. Relief of symptoms was only temporary. Two attacks of asthmatic bronchitis required hospitalization for approximately two weeks for two consecutive years.

During the winter of 1930 he had recurrent attacks of asthma several times a week. The attacks continued throughout the next year, and in May 1932 he had a severe attack of asthmatic bronchitis, which required hospitalization. Epinephrine was not tolerated and caused extreme nervousness and a fluctuation of blood pressure, which reached as high as 190 systolic and 100 diastolic. An

9. Cole, H. N.; DeWolf, J.; McCuskey, J. M.; Miskjian, H. G.; Williamson, G. S.; Rauschkolb, J. R.; Ruck, R. O., and Clark, T.: Toxic Effects Following Use of the Arsphenamines, J. A. M. A. **97**:897-904 (Sept. 26) 1931.

10. Strickler, A.; Munson, H. G.; Sidlich, D. M., and Strauss, A.: Clinical Study of Reactions Following Intravenous Administration of Arsphenamin in Nonsyphilitic Persons, Arch. Dermat. & Syph. **2**:692-698 (Dec. 20) 1920.

11. Cole, H. N., and others: Cooperative Clinical Studies in the Treatment of Syphilis: Arsenical Reactions, Ven. Dis. Inform. **14**:173-200 (Aug.) 1933.

12. Phelps, J. R., and Washburn, W. A.: Toxic Effects of Arsenical Compounds Employed in the Treatment of Syphilis in the United States Navy: A Statistical Study of the Results of 272,354 Injected Doses of Neoarsphenamine and Other Compounds of Arsenic, Urol. & Cutan. Rev. **34**:458-476 (July) 1930.

oxygen tent was used, and dextrose and sodium iodide were administered intravenously. The patient also received amytal and sedatives and steam inhalations of compound tincture of benzoin U. S. P. On being dismissed from the hospital, he was referred to an allergist for a complete investigation. With a program of management for allergy, his respiratory symptoms improved from 75 to 90 per cent.

The patient gave a further history of having had severe hives and angioneurotic edema following injection of streptococcus antiserum to control a chronic sore throat from which hemolytic streptococci had been grown in pure cultures. He had also had attacks of migraine headache associated with scotoma and nausea, which had been controlled by rest in bed and ergotamine tartrate.

In the past, mild transitory attacks of atopic dermatitis had involved both the popliteal and the cubital fossae during the summer months. The use of certain soaps and toilet products had also caused contact dermatitis.

The history revealed, further, that this patient had had recurrent attacks of asthma when he was working in the outpatient department of a large hospital. Later, in private practice, he found that in treating syphilitic patients with neoarsphenamine he would experience sneezing, wheezing and frank asthma. Symptoms occurred within two minutes after he opened an ampule of neoarsphenamine. If the nurse mixed the drug in a separate room and brought it to him in a syringe ready for administration, he would have no symptoms.

On his own initiative the patient had considered the possibility of oral hyposensitization to neoarsphenamine. He prepared a solution containing approximately 3 mg. of the drug to ½ drachm (1.8 cc.) and took it orally. About twenty minutes after taking the 3 mg. dose he experienced slight wheezing and a feeling of tightness in the chest. The symptoms rapidly developed into severe asthma with cyanosis, for which he was given 0.5 cc. of a 1 to 1,000 solution of epinephrine hydrochloride. He was hospitalized and placed in an oxygen tent. Small doses of epinephrine hydrochloride solution (1 : 1,000) were given at intervals of every few minutes until the severe reaction had passed. Forty-eight hours elapsed before the attack was controlled completely.

A patch test with arsphenamine showed at the end of twenty-four hours a definite area of cutaneous involvement 1 cm. in diameter characterized by erythema, roughness and small vesicles in the center. The patient stated that he was conscious of slight itching and discomfort from the patch test. The reaction from the patch test persisted for several weeks and was characterized by yellow discoloration and roughness.

Physical Examination.—The results of general physical examination on his admission to the clinic were essentially normal. Examination of the nose and throat revealed a slight nasal discharge and a slight deviation of the nasal septum to the left. The turbinates were decidedly swollen, pale gray and boggy in appearance.

Laboratory Studies.—Study of the blood revealed eosinophilia, with 12 per cent eosinophils. A roentgenogram of the chest showed a slight increase in the hilar thickening. A roentgenogram of the nasal sinuses was normal.

Allergy Investigation.—Repeated investigations for allergy were carried out, and significant reactions were found to dust, orris root, kapok, mattress dust and some of the molds. Some of the foods were definitely incriminated as causing symptoms, and others elicited false positive reactions. Certain bacteria and a stock respiratory vaccine elicited positive reactions. There were no significant reactions to pollen.

The patient knew that the following allergens produced either rhinitis or asthma or both: kapok, dust, tobacco smoke and ashes and orris root and, among foods, chocolate, beer, ale and alcohol in any form. Gastrointestinal symptoms characterized by cramps and liquid stools containing considerable mucus at times followed the ingestion of beans, cabbage and brussels sprouts.

A program of management for allergy was outlined and has been followd with satisfactory results for three years. Exacerbations of the rhinitis, asthma, gastrointestinal symptoms, migraine and other symptoms occur if the patient does not follow his diet carefully. No hyposensitization treatment is being given at present.

COMMENT

This case illustrates the occurrence of sensitivity to a drug in a person with multiple manifestations of allergy, including bronchial asthma, perennial allergic rhinitis, migraine, gastrointestinal allergy, atopic dermatitis, contact dermatitis and a history of urticaria and angioneurotic edema. It further illustrates the danger of attempting oral hyposensitization in cases of drug allergy by the administration of small doses of the drug.

Neoarsphenamine and other forms of arsphenamine should never be considered in the subsequent treatment of this patient, even though he should contract syphilis or some other condition for which such drugs are used. The reaction to a patch test with the drug was positive, and a definite constitutional reaction was precipitated by the ingestion of a minimal amount of arsphenamine.

Dr. George Curtis, of the Department of Dermatology, contributed certain historical data.

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DERMATITIS HERPETIFORMIS

IMMUNOLOGIC AND THERAPEUTIC CONSIDERATIONS

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The purpose of this paper is to evaluate the treatment of dermatitis herpetiformis with various sulfonamide compounds and to report studies which may have some bearing on the pathogenesis of the disease.

In 1938 one of us (J. H. S.), in studying immunologic response in cases of dermatitis herpetiformis, found that intradermal injection of Bacterium coli vaccine produced lesions simulating those of dermatitis herpetiformis at the site of injection. The favorable results obtained with sulfonamide compounds prompted us to continue the immunologic studies. As a further study of the pathogenesis of dermatitis herpetiformis chemical studies of the blood serum were undertaken.

In this paper we therefore present the findings of immunologic and chemical studies and in addition report the therapeutic results obtained with drugs of the sulfonamide group.

IMMUNOLOGIC STUDIES

The effects obtained with sulfonamide compounds in dermatitis herpetiformis stimulate speculation as to the cause of this disease. The fact that some sulfonamide compounds improve the lesions of dermatitis herpetiformis but not those of pemphigus suggests that dermatitis herpetiformis and pemphigus are not closely related.

Review of the Literature.—The frequently observed aggravation of the eruption of dermatitis herpetiformis after ingestion of iodides or bromides has suggested an allergic factor in the causation of the disease to such observers as Jadassohn,[1] Riecke,[2] Darier and Tzanck.[3] Yet

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1. Jadassohn, J., in discussion on Jessner, M., and Hoffmann, H.: Jod- und Bromempfindlichkeit bei Dermatitis herpetiformis und Pemphigus, Klin. Wchnschr. **5**:124, 1926.

2. Riecke, E.: Dermatitis herpetiformis, in Jadassohn, J.: Handbuch für Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 7, pt. 2, p. 614.

3. Darier, J., and Tzanck, A.: Pemphigus und Dermatitis Duhring und die sogenannten Uebergangsfälle, Dermat. Wchnschr. **100**:73, 1935.

the response of dermatitis herpetiformis to sulfonamide compounds would suggest a bacterial factor in the causation of the disease. The possibility that dermatitis herpetiformis may be a manifestation of a bacterial allergy has been considered by several observers.

Bernhardt,[4] in 1935, performed on patients with dermatitis herpetiformis intradermal tests with staphylococcus vaccine, streptococcus vaccine, trichophytin and tuberculin. The tests with staphylococcus vaccine produced an erythematopapular reaction in all 8 patients tested. The tests with streptococcus vaccine produced reactions in 7 out of 8 patients; in 3 of them the reaction was erythematovesicular. The tests with trichophytin elicited a reaction in 5 out of 6 patients; in 3 instances the reaction was erythematovesicular. Tuberculin caused an erythematopapular reaction in all patients tested. Bernhardt obtained also a vesicular reaction with streptococcus vaccine, staphylococcus vaccine and tuberculin in 2 out of 3 patients with pemphigus vulgaris. His conclusion was that both dermatitis herpetiformis and pemphigus were sensitization dermatoses.

Leone[5] obtained bullous reactions to intradermal injections of streptococcus vaccine, living streptococci, staphylococcus vaccine, living staphylococci and gonococcus vaccine in patients with dermatitis herpetiformis. He, however, did not attribute any etiologic significance to these reactions but regarded them as isomorphous reactions analogous to Köbner's phenomenon in psoriasis.

One of us (J.H.S.),[6] in the discussion of Goodman's paper, reported the production of dermatitis-herpetiformis-like lesions—namely, grouped vesicles on an erythematous base—in patients with dermatitis herpetiformis by intradermal injections of 0.1 cc. of a Bact. coli vaccine prepared from the patient's stool. No such vesicular reactions were observed following intradermal injections of Streptococcus faecalis vaccine.

Callaway and Sternberg[7] obtained in 1 patient with dermatitis herpetiformis bullous reactions to intradermal and patch tests with an autovaccine prepared from pneumococci of type VII. By subsequent injections of the vaccine they were able to desensitize the patient to this strain of pneumococcus and to obtain clinical improvement. These authors expressed the belief that bacterial allergy was an etiologic factor in this case of dermatitis herpetiformis.

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4. Bernhardt, R.: Weitere Beiträge zur Ätiologie des Pemphigus und der Duhringschen Krankheit, Arch. f. Dermat. u. Syph. **171**:536, 1935.

5. Leone, R.: Dermatite erpetiforme e streptococco, Gior. ital. di dermat. e sif. **79**:365, 1938.

6. Swartz, J. H., in discussion on Goodman, M. H.: Dermatitis Herpetiformis, Arch. Dermat. & Syph. **43**:254 (Feb.) 1941.

7. Callaway, J. L., and Sternberg, T. H.: Bacterial Allergy: An Etiologic Factor in Dermatitis Herpetiformis, Arch. Dermat. & Syph. **43**:956 (June) 1941.

Results of Immunologic Studies.—Twelve patients with dermatitis herpetiformis and 20 patients with other cutaneous diseases were tested with intradermal injections of 0.1 and 0.2 cc. of Bact. coli vaccine, streptococcus vaccine, staphylococcus vaccine, staphylococcus toxoid, snake venom and physiologic solution of sodium chloride. Various strains of B. coli, streptococci and staphylococci were employed for the preparation of vaccines: B. coli from the stools of patients with dermatitis herpetiformis, of normal persons and of patients with other cutaneous diseases; streptococci from the stools of patients with dermatitis herpetiformis and of patients with other cutaneous diseases, and staphylococci from suppurative cutaneous lesions.

It was found that in the 20 patients with cutaneous diseases other than dermatitis herpetiformis the intradermal tests with 0.1 to 0.2 cc. of physiologic solution of sodium chloride and snake venom did not show a

Fig. 1.—Right arm of patient M. S. (diagnosis, dermatitis herpetiformis). The upper papular lesion is a forty-eight hour reaction to an intradermal injection of 0.1 cc. of autogenous Str. faecalis vaccine; the lower vesicular lesion is a reaction to 0.1 cc. of autogenous Bact. coli vaccine.

reaction after twenty-four hours, while the vaccines prepared from Bact. coli, streptococci and staphylococci when injected intradermally in the aforementioned doses frequently produced a papular reaction, often with a central pustule, surrounded by an area of erythema.

Seven of the 12 patients with dermatitis herpetiformis responded with the aforedescribed reactions. A vesicular reaction was obtained by the injection of Bact. coli vaccine in 5 patients. The reactions consisted of groups of vesicles on an inflammatory base at the site of injection. These 5 patients reacted with vesicular lesions to all strains of Bact. coli irrespective of the source of the strain (figs. 1 and 2). One of them had a vesicular reaction also to the staphylococcus vaccines (fig. 3) and 1 to the streptococcus vaccines.

It appears significant that 42 per cent of the patients with dermatitis herpetiformis responded with the formation of multiple vesicles to injections of Bact. coli vaccines. The fact, however, that 1 patient showed a vesicular reaction also to the streptococcus vaccines and another to the staphylococcus vaccines suggests that the vesicular reaction in patients with dermatitis herpetiformis is not limited to Bact. coli.

Our observations agree essentially with those of Bernhardt, Leone and Callaway and Sternberg, namely, that patients with dermatitis

Fig. 2.—Upper part of back of patient F. D. (diagnosis, dermatitis herpetiformis). The intradermal injections of 0.1 cc. of various Bact. coli vaccines have produced vesicular reactions, whereas injections of physiologic solution of sodium chloride, staphylococcus toxoid, staphylococcus vaccine, snake venom, typhoid vaccine and Str. faecalis have produced either no reactions or only papular reactions. The following reactions were caused by injections of Bact. coli vaccine: second row, tests 2, 3, 5 and 6; third row, tests 2, 4, 5 and 6; fourth row, tests 1 and 2. The following reactions were caused by injections of Str. faecalis: second row, test 4; third row, tests 1 and 3.

herpetiformis frequently respond with formation of vesicles to intradermal injections of bacterial vaccines, except that we have found a vesicular reaction to occur most frequently to Bact. coli. It seems reasonable to us to regard the vesicular reaction as an expression of bacterial allergy,

as Bernhardt and Callaway have done, and not merely as an isomorphous response similar to the Köbner phenomenon, as Leone has done. If it were the latter, a vesicular response would have followed also the injections of snake venom and physiologic solution of sodium chloride. The assumption that bacterial allergy is the cause of dermatitis herpetiformis would explain the favorable response to some of the sulfonamide compounds.

CHEMICAL STUDIES OF THE BLOOD SERUM

Review of the Literature.—Few chemical studies of the blood serum from patients with dermatitis herpetiformis have been reported. The

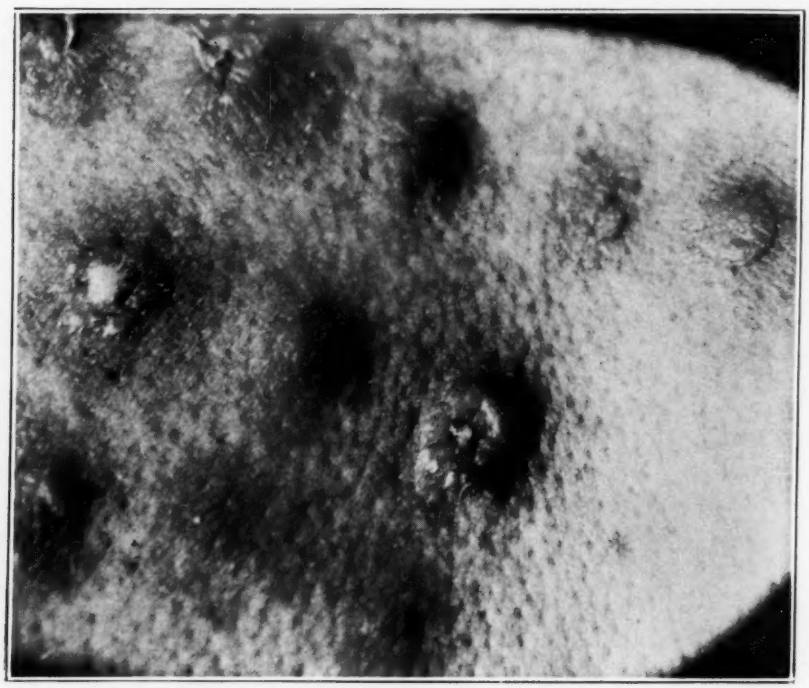

Fig. 3.—Upper part of back of patient P. H. (diagnosis, dermatitis herpetiformis). Vesicular reactions were obtained to injections of Bact. coli and staphylococcus vaccine and papular reactions only to injections of Str. faecalis vaccine. The following reactions were caused by Bact. coli vaccine: first row, tests 1, 2, 4 and 5; second row, tests 1 and 3. The following reactions were caused by injections of Str. faecalis vaccine: first row, test 3; second row, test 2. Staphylococcus vaccine produced the vesicular reaction in the third row, test 1. Staphylococcus toxoid produced the erythematous reactions in the third row, tests 2 and 3.

sodium chloride is the only constituent of which determinations have been published by previous investigators. The values of these determinations vary over a wide range, some values being below and others above normal.

Urbach [8] determined the sodium chloride in the blood serum of 2 patients with dermatitis herpetiformis. Normal values for sodium chloride with the method employed were stated by him to be 560 to 600 mg. per hundred cubic centimeters. The first patient had an elevated sodium chloride content at the time of exacerbation, 637 mg. per hundred cubic centimeters. The second patient had a normal sodium chloride concentration during both an exacerbation and a remission, i. e., 592 and 598 mg. respectively. Von Leszczynski and Blatt [9] reported determinations of sodium chloride in the blood serum of 2 patients with dermatitis herpetiformis. The first patient (tables 11 and 13 in their report) had a "markedly decreased" sodium chloride level on seven occasions; the second patient (table 12 in their report) had a "decreased" sodium chloride level on four occasions. The values of their determinations were not quoted in their publication. Bernhardt carried out determinations of sodium chloride in the blood serum of 10 patients with dermatitis herpetiformis. In a first paper [10] he reported the values of sodium chloride in 2 patients as 397 and 525 mg. per hundred cubic centimeters respectively; in a second paper,[4] the values of sodium chloride in 8 patients were 610, 640, 671, 642, 642, 584, 584 and 525 mg. per hundred cubic centimeters respectively. The author did not give the range of normal values with his method and did not comment on his determinations. It would seem that the variations are rather wide. For these reasons an evaluation is impossible. Turpin and Chassagne [11] performed chemical studies of the blood in a case of Duhring-Brocq disease, which in America, however, would probably be regarded as a case of pemphigus vulgaris, since there were large bullae and the disease was fatal. They found a moderate hypoproteinemia with a reversal of the albumin-globulin ratio, lowered calcium and sodium values but an elevated potassium level in the blood serum. All these changes have been previously reported by one of us (W.F.L.) as occurring frequently in pemphigus.[12]

Results of Chemical Determination.—Chemical studies of the blood were carried out on 15 patients with dermatitis herpetiformis. The following constituents were determined: total fixed base, sodium, potassium, calcium, chlorides, protein, phosphates, uric acid and nonprotein nitrogen. The methods of determinations were those described

8. Urbach, E.: Zur Pathochemie des Pemphigus, Arch. f. Dermat. u. Syph. **150**:52, 1926.

9. von Leszczyński, R., and Blatt, O.: Pemphigusstudien mittels der Kochsalzquaddel, Arch. f. Dermat. u. Syph. **153**:307, 1927.

10. Bernhardt, R.: Zur Ätiologie des Pemphigus und der Duhringschen Krankheit, Acta dermat.-venereol. **14**:165, 1933.

11. Turpin, R., and Chassagne, P.: Etude de la maladie de Duhring-Brocq. Son syndrome physico-chimique, Ann. de dermat. et syph. **10**:862, 1940.

12. Talbott, J. H.; Lever, W. F., and Consolazio, W. F.: Metabolic Studies on Patients with Pemphigus, J. Invest. Dermat. **3**:31, 1940.

by Talbott.[13] The values were within the range of normal with the exception of the values for serum sodium, which were above normal in 4 out of 11 patients, as shown in the accompanying table. While the normal range for sodium with the method used [14] is 139 to 141 milliequivalents per liter, values above 145 milliequivalents per liter were obtained for 4 patients. Although not all the values for sodium in these 4 patients were abnormally high, the average reading was 142.8

Concentration of Various Constituents in the Blood Serum of Fifteen Patients with Dermatitis Herpetiformis

		Total Base *	Sodium *	Potassium *	Calcium *	Chlorides *	Protein †	Uric Acid ‡	Phosphates ‡	Nonprotein Nitrogen ‡
Normal values.....		150-155	139-141	4-5	4.7-5.4	102-106	6.4-7.5	3-5	3.1-4.5	20-35
F. M.	11/14/39	156.5	142.8	4.40	5.44	102.5	7.13	....	2.32	23.4
	11/21/39	151.3	138.0	....	5.26	.....	7.01	....	....	....
	12/16/39	.....	.....	....	....	.....	7.20	....	....	....
	2/10/40	.....	138.8	....	4.84	.....	6.70	....	2.50	31.5
	1/24/42	.....	146.5	....	....	106.6	....	....	....	....
	2/ 4/42	.....	143.5	....	....	.....	....	....	....	....
C. F.	5/19/39	153.0	.....	....	5.43	.....	8.51	5.52	4.18	28 0
	5/ 1/40	.....	139.5	....	4.89	.....	8.04	....	....	23.8
	4/ 2/40	148.0	137.0	4.40	4.81	103.4	7.04	....	3.23	26.4
B. F.	5/ 3/39	152.6	.....	....	4.41	.....	5.54	5.08	....	....
	5/ 6/39	.....	.....	....	4.72	.....	....	....	....	....
S. G.	5/24/39	155.7	.....	....	5.06	.....	7.18	4.20	....	....
J. K.	5/ 5/38	.....	.....	....	....	103.0	....	....	....	....
	5/12/38	.....	.....	....	....	100.0	....	....	....	....
D. R.	5/ 2/39	.....	.....	....	5.12	.....	....	....	....	....
L. C.	7/ 1/36	151.0	141.4	....	....	102.0	....	....	....	....
F. D.	2/26/40	152.5	137.5	3.98	4.84	.....	7.63	....	....	25.8
	1/28/42	.....	145.0	....	....	100.5	....	....	....	....
L. W.	4/23/41	.....	146.5	....	5.24	.....	7.23	....	....	....
D. T.	8/26/41	.....	143.4	....	....	.....	....	....	....	24.0
G. G.	8/26/41	.....	141.7	....	....	.....	....	....	....	21.0
P. H.	8/29/41	.....	141.4	....	....	.....	....	....	....	31.8
M. S.	8/ 2/41	.....	147.4	4.70	4.96	105.1	7.09	....	....	25.3
	1/24/42	.....	142.0	....	....	102.6	....	....	....	....
	1/31/42	.....	142.8	....	....	.....	....	....	....	....
L. H.	1/28/42	.....	141.5	....	....	103.9	....	....	....	....
R. E.	2/ 4/42	.....	140.7	....	....	102.4	....	....	....	....
Average values.....		152.6	142.0	4.37	5.00	102.9	7.19	4.93	3.06	26.1

* Expressed in milliequivalents per liter.
† Expressed in grams per hundred cubic centimeters.
‡ Expressed in milligrams per hundred cubic centimeters.

milliequivalents per liter. The average value in all the 11 cases was 142 milliequivalents per liter.

THERAPEUTIC STUDIES

Review of the Literature.—The use of sulfonamide compounds in treatment of dermatitis herpetiformis has been reported by several

13. Talbott, J. H.: Interpretation of Clinical Chemical Procedures, Ohio State M. J. **35**:137, 1939.

14. Butler, A. M., and Tuthill, E. J.: An Application of the Uranyl Zinc Acetate Method for Determination of Sodium in Biological Material, J. Biol. Chem. **93**:171, 1931.

authors since the first report by Lain and Lamb [15] in 1938. However, only two reports are in the form of papers, both of which appeared in the Spanish literature, recording only 1 case each.[16] All the other reports are in the form of case presentations at meetings of dermatologic societies. The review of the literature is necessarily incomplete, since the recent European literature has not been accessible because of the war.

Fifteen cases of dermatitis herpetiformis in which sulfanilamide was administered have been reported in the American literature up to December 1941. Five additional cases have been found in the foreign literature, making a total of 20. Sulfanilamide proved beneficial in 14 of these 20 cases, of doubtful value in 4 and of no value in 2. In the reports of 9 of the 14 cases in which sulfanilamide was effective it was pointed out that the response was merely temporary. The other 5 cases were reported too soon to permit evaluation as to whether the benefit was temporary or permanent. Only 3 cases of dermatitis herpetiformis in which sulfapyridine was given have thus far been reported. In all 3 a satisfactory response was obtained.

The American authors who obtained good results with sulfanilamide were the following: Lain and Lamb [15] reported almost complete clearing in 1 patient. Butterworth [17] saw a good response in 1 case. Lewis [18] saw substantial improvement in 2 patients, who at the time of the report had remained well without treatment for five weeks and for six months, respectively. Abramowitz [19] saw "rather dramatic improvement" in 3 cases. Miller [20] reported a case of severe dermatitis herpetiformis which cleared entirely but recurred two months after treatment was discontinued. In the foreign literature Sainz de Aja [16a] and Caseaux [16b] reported temporary clearing in 1 case each, Caseaux calling the effect magnificent. Wolfram [21] obtained considerable improvement in 1 case within five days. Ruding [22] and Wiersema [23] also obtained improvement, which continued only as long as the drug was given.

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15. Lain, E. S., and Lamb, J. H.: Treatment of a Pemphigoid Eruption with Sulfanilamide, Arch. Dermat. & Syph. **37**:840 (May) 1938.

16. (*a*) Sainz de Aja, E. A.: Linfogranulomatosis inguinal, dermatitis de Duhring y prontosil, Actas dermo-sif. **30**:207, 1939. (*b*) Caseaux, D. C.: Dos casos de linfogranulomatosis inguinal subaguda y uno de dermatitis de Duhring, tratados con derivados sulfamidicos, ibid. **31**:98, 1939.

17. Butterworth, T., in discussion on Schildkraut, J. M.: A Case for Diagnosis (Dermatitis Herpetiformis?), Arch. Dermat. & Syph. **40**:650 (Oct.) 1939.

18. Lewis, G. M.: Dermatitis Herpetiformis (Treated with Sulfanilamide); Arsenical Keratosis, Arch. Dermat. & Syph. **42**:961 (Nov.) 1940.

19. Abramowitz, E. W., in discussion on Lewis.[18]

20. Miller, H. E., in discussion on Epstein, N. N.: Dermatitis Herpetiformis, Arch. Dermat. & Syph. **43**:883 (May) 1941.

21. Wolfram, S.: Pemphigus pruriginosus, Dermat. Wchnschr. **111**:607, 1940.

22. Ruding, J.: Morbus Duhring, Dermat. Wchnschr. **110**:345, 1940.

23. Wiersema, M. U.: Dermatitis herpetiformis, Dermat. Wchnschr. **110**:527, 1940.

Doubtful response to sulfanilamide was obtained by Combes and Cañizares [24] in 3 cases and by Epstein [25] in 1 case. Pillsbury [26] and Costello [27] regarded sulfanilamide as a failure in 1 case each.

Costello [28] treated with sulfapyridine the patient who had failed to respond to sulfanilamide. The skin cleared after two weeks and no further treatment was given. After seven months there had been no recurrence. Oliver and Cohen [29] obtained complete clearing of the skin with sulfapyridine in 1 patient after ten days of treatment. The patient was still free from lesions after six months. A patient of Senear and Perlstein [30] responded to sulfapyridine on three occasions but relapsed each time when administration of the drug was discontinued.

Inasmuch as herpes gestationis is considered by many authorities to be a variety of dermatitis herpetiformis, it seems worth mentioning that in 3 cases of herpes gestationis no benefit was obtained from the administration of sulfonamide compounds. Mayr [31] administered uliron (N^1-N^1-dimethyl-N^4-sulfanilylsulfanilamide), Barney [32] sulfanilamide and Turner and Zakon [33] sulfanilamide as well as sulfapyridine without evidence of improvement. This lack of response would suggest a different etiologic basis for the two diseases, but the number of reported cases is too small to permit one to draw any definite conclusions.

Therapeutic Results.—Thirteen patients with dermatitis herpetiformis have been treated with various sulfonamide compounds since October 1939 in the dermatologic clinic of the Massachusetts General Hospital. Every patient has been under observation for a minimum of ten months. Ten patients were males; 3, females. Sulfanilamide and sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) were uniformly effective in the 13 reported cases, sulfapyridine being in

24. Combes, F. C., and Cañizares, O.: Sulfanilamide and Allied Compounds, Arch. Dermat. & Syph. **44**:236 (Aug.) 1941.

25. Epstein, N. N.: Dermatitis Herpetiformis, Arch. Dermat. & Syph. **38**:985 (Dec.) 1938.

26. Pillsbury, D. M.: Dermatitis Herpetiformis, Arch. Dermat. & Syph. **38**:985 (Dec.) 1938.

27. Costello, M.: Dermatitis Herpetiformis Treated with Sulfapyridine, Arch. Dermat. & Syph. **41**:134 (Jan.) 1940.

28. Costello, M.: Dermatitis Herpetiformis Treated Successfully with Sulfapyridine, Arch. Dermat. & Syph. **42**:161 (July) 1940.

29. Oliver, E. A., and Cohen, T. M.: Dermatitis Herpetiformis, Arch. Dermat. & Syph. **44**:303 (Aug.) 1941.

30. Senear, F. E., and Perlstein, M., in discussion on Omens, O. V.: Dermatitis Herpetiformis, Arch. Dermat. & Syph. **43**:1065 (June) 1941.

31. Mayr, J.: Zur Frage der Schwangerschaftsunterbrechung beim Herpes gestationis, München. med. Wchnschr. **87**:742, 1940.

32. Barney, R. E.: Dermatitis Herpetiformis (Herpes Gestationis), Arch. Dermat. & Syph. **44**:129 (July) 1941.

33. Turner, S. J., and Zakon, S. J.: Herpes Gestationis, Am. J. Obst. & Gynec. **41**:525, 1941.

general superior to sulfanilamide. Sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) exerted some beneficial effect on the symptoms and lesions of dermatitis herpetiformis, while sulfadiazine (2-[paraaminobenzenesulfonamido]-pyrimidine) and sulfaguanidine (sulfanilylguanidine) appeared to be ineffective. Objective improvement usually was evident within two or three days after treatment with sulfapyridine or sulfanilamide was begun. Itching was often considerably relieved within twelve hours. The improvement was, however, only temporary. Discontinuance of administration of sulfapyridine or sulfanilamide was followed by a recurrence of both subjective and objective symptoms within a day or two; but by continued use of the drug it was possible in all cases to keep the eruption in check. In cases of the more severe form of the disease complete clearing of the lesions could not be obtained, but the itching was decreased to such an extent that the patients could be persuaded only with difficulty to stop taking the drug even for only a few days. In order to control the eruption of dermatitis herpetiformis, daily administration of sulfonamide compounds was necessary during the active stage. As patients with the more severe forms of the disease had new lesions day after day without appreciable remissions, sulfapyridine was given to them continuously for many months. Two of the patients reported on (cases 1 and 2) have been taking sulfapyridine daily for over two years. Since with the milder forms of dermatitis herpetiformis there were spontaneous remissions, it was possible to stop the use of sulfonamide compounds for periods of various length, but there was no reason to assume that these remissions were induced by the drug.

Dosage.—The amount of medication required to keep the eruption of dermatitis herpetiformis in check varied in different patients and with the severity of the disease. In no case was it necessary to prescribe more than 3 Gm. of sulfapyridine per day; patients with the milder forms often did well with as little as 1 Gm. a day. When sulfanilamide was given, the dosage had to be larger, often 4 Gm. a day. In some cases sulfanilamide even in doses larger than those of sulfapyridine produced less satisfactory results. Determination of the sulfanilamide or sulfapyridine in the blood showed that the symptoms of dermatitis herpetiformis could be controlled with low concentrations of the drugs. With sulfanilamide optimal relief was usually experienced with a blood level of 2 mg. per hundred cubic centimeters; with sulfapyridine a trace was often sufficient.

Toxicity.—In 2 of the 13 patients (cases 1 and 4) sulfanilamide caused a morbilliform eruption with edema of the face and hands. One of the 2 patients (case 1) subsequently tolerated sulfapyridine well. The other patient (case 4) was not given further medication with any sulfonamide drug because of the severity of the eruption.

No cutaneous eruption was observed following treatment with sulfapyridine in any of the 13 patients given this drug. Nausea occurred in 2 patients (cases 6 and 9). In 1 of them (case 9) the nausea followed the use of sulfapyridine and was severe enough to prevent its further administration. After five months the patient was able to tolerate small doses of the drug. In the other patient (case 6) in whom the nausea was caused by sulfanilamide, small doses of sulfanilamide and sulfapyridine were tolerated fairly well. Weekly blood counts and smears were made in all cases for the first few weeks and at greater intervals thereafter. In none of them were there pathologic changes found at any time.

REPORT OF CASES

The first 2 cases are reported in detail because they serve to illustrate the effects of the various sulfonamide compounds in patients with severe dermatitis herpetiformis. Both patients have received sulfonamide compounds continuously for more than two years.

CASE 1.—M. S., a man aged 24, of English-Canadian descent, was seen first in November 1939, presenting a widespread eruption characteristic of dermatitis herpetiformis. Since its onset in June 1938 there had never been any appreciable remission. The administration of 4 Gm. of sulfanilamide daily was started on Nov. 3, 1939. Within three days there was considerable improvement of the eruption and practically no itching. After five days the patient showed only a few active lesions. The administration of sulfanilamide was stopped after ten days of treatment. On the third day new lesions began to appear. Medication with 2 Gm. of sulfanilamide daily was resumed. On the fourth day after resumption of treatment no new lesions were noticed. On the tenth day erythema and swelling of the face and hands developed and a generalized morbilliform eruption, which was regarded as a toxic eruption due to sulfanilamide.

Use of the drug was stopped and solution of potassium arsenite U. S. P. prescribed. Under this medication the dermatitis herpetiformis gradually became worse, and administration of 4 Gm. of sulfapyridine a day was begun on Dec. 27, 1939. The next day the patient felt more comfortable, and from the third day on he was practically asymptomatic. After ten days the dose was reduced to 3 Gm. a day. At the time of writing the patient has been under continuous daily treatment with sulfapyridine for more than two years. The daily amount necessary to check the eruption has varied between 2 and 3 Gm. With this amount small crops of lesions appear occasionally but cause less itching. Failure to take sulfapyridine for even as long as one day causes considerable aggravation of the eruption and severe itching. There were no toxic symptoms from sulfapyridine. Sulfaguanidine, 3 Gm. a day, was substituted for the sulfapyridine for a few days in order to determine its effectiveness, but its use had to be stopped because it did not seem to control the disease. Similar results were experienced with sulfadiazine. Sulfathiazole, 3 Gm. a day, produced some symptomatic improvement and a reduction in the number of new lesions but no results comparable to those obtained by the administration of sulfapyridine.

During the entire period the level of sulfanilamide and sulfapyridine in the blood was determined at regular intervals and usually only a trace was found. The highest level of sulfanilamide was 2.9 mg. per hundred cubic centimeters and of sulfapyridine 1.6 mg.

CASE 2.—F. M., a man aged 27, of Italian descent, presented himself in December 1938 with a widespread eruption of dermatitis herpetiformis, which had begun in April 1938. He stated that he had had occasional short periods of spontaneous improvement. From December 1938 to November 1939 he was treated with solution of potassium arsenite U. S. P., 15 drops daily. This checked the eruption only to a limited degree, and exacerbations occurred several times during this medication. In November 1939, when the patient had a severe relapse, the treatment was changed to 4 Gm. of sulfanilamide a day. The next day the itching had almost subsided and the number of new lesions was greatly diminished. On the fifth day the patient was practically free from subjective and objective symptoms. On the tenth day the dose was reduced to 3 Gm. per day. While he took the reduced dose new lesions occasionally developed but itching was not pronounced. During the following months the daily dose varied between 2 and 4 Gm., as was needed by the patient to control the eruption. Daily doses of 2 Gm. of sulfapyridine were begun in February 1940. This amount controlled the eruption most of the time. Occasionally, he had to take 2.5 Gm. in order to be comfortable. Medication with sulfapyridine, the dose varying between 2 and 2.5 Gm. a day, has been continued up to the time of writing, a period of more than two years.

Sulfaguanidine proved to be of no value, even in doses of 4.5 Gm. a day. The patient became decidedly worse on the second day after starting treatment with this drug. The results with sulfadiazine were just as unsatisfactory.

There were never any toxic symptoms from any of the sulfonamide drugs. The level of sulfanilamide in the blood varied between 3.7 and 5.9 mg. per hundred cubic centimeters; the level of sulfapyridine varied between a trace and 4.2 mg. Even with only a trace of sulfapyridine, the patient felt comfortable.

CASE 3.—R. E., a man aged 37, an American, was first seen in July 1941 with an extensive eruption of dermatitis herpetiformis of nine months' duration. Sulfathiazole, 3 Gm. a day, was given for one week, with no relief. Use of sulfapyridine in doses of 3 Gm. a day was then started. This resulted in improvement of the lesions and relief from itching within three days. The patient has been treated with sulfapyridine (2.5 to 3 Gm. a day) up to the present time, and, although occasionally small crops of lesions have appeared, he has been comfortable. Failure to take sulfapyridine even for one day resulted in exacerbations. There were never any toxic symptoms. Sulfaguanidine was tried and found completely ineffective. The level of sulfapyridine in the blood was never more than a trace.

CASE 4.—C. F., a man aged 47, of Irish descent, reported to the dermatologic clinic in February 1937 with an extensive eruption of dermatitis herpetiformis of four years' duration. Although he had periods of exacerbations and remissions, he was at no time completely free from lesions. Treatment with solution of potassium arsenite U. S. P., bismuth compounds and bismarsen proved ineffective.

In April 1940 the administration of sulfathiazole was begun. Four grams was given daily for thirteen days, resulting in some improvement. Sulfapyridine was then given, 1.5 Gm. a day. This was followed by striking improvement within four days. But after three weeks the patient experienced lassitude, anorexia and headache to such a degree that the use of sulfapyridine had to be discontinued. The patient was without treatment for four weeks, during which time numerous lesions again broke out.

He was then given sulfanilamide, 4 Gm. a day, which produced a considerable improvement within three days. During the following two months he received

daily doses of 2 to 4 Gm. of sulfanilamide. Four grams checked the eruption satisfactorily, but with smaller doses occasional new crops of lesions appeared. After two months of treatment, in August 1940, a widespread toxic eruption suddenly developed, which obviously was caused by the drug. The patient has not received any sulfonamide compound since.

The level of sulfathiazole in the blood was 2 mg. per hundred cubic centimeters after thirteen days of treatment. The level of sulfanilamide varied between a trace and 1.7 mg.; that of sulfapyridine was never more than a trace.

Case 5.—F. D., a man aged 39, an American, had had dermatitis herpetiformis since December 1939. He reported in February 1940. Because of a widespread eruption typical of dermatitis herpetiformis, sulfanilamide, 4 Gm. a day, was administered, and there was rapid improvement. On the twelfth day the dose was reduced to 3 Gm. a day. This dosage was continued until April 1941. From April to August 1941 he was treated with sulfapyridine, 1.5 to 2 Gm. a day. After August 1941 no further treatment was necessary because there were few lesions. It is believed that the long remission in this case was not due to the drug.

The highest level of sulfanilamide obtained was 4.6 mg. per hundred cubic centimeters; that of sulfapyridine was never more than a trace.

Case 6.—A. S., a man aged 64, an Italian, in whom dermatitis herpetiformis developed in August 1938, reported for treatment in November 1939, when the administration of sulfanilamide, 4 Gm. a day, was started. Within one week almost complete remission was noted. This dose resulted in gastric distress and diarrhea. Smaller doses were tolerated but did not control the eruption completely. In March 1940 the use of sulfapyridine, 1.5 Gm. daily, was started. This was tolerated and kept the patient comfortable. From May 1940 to January 1941 the patient did not return because he had a remission. From then on his visits to the clinic were few and far between because he felt that further treatment was not necessary. He visited the clinic a few times early in 1941, when he showed few vesicles. He has not been seen since May 1941.

The highest level of sulfanilamide obtained was 6.1 mg. per hundred cubic centimeters; that of sulfapyridine was never more than a trace.

Case 7.—M. C., a Jew aged 48, had suffered from dermatitis herpetiformis since 1937. The eruption was moderately severe with periods of spontaneous remission during which only a few lesions appeared. At the time of an exacerbation, in October 1940, sulfapyridine, 1.5 Gm. per day, was prescribed. Improvement followed within a few days. The patient continued to take this amount for four months, until February 1941. Since then he has needed only 0.5 to 1 Gm. per day in order to keep himself comfortable, and at times he has been able to discontinue taking the medication for several weeks.

Case 8.—M. B., an Italian woman aged 46, with a moderately severe dermatitis herpetiformis since August 1938, was given sulfanilamide, 2 Gm. a day, beginning in October 1939. Within three days there was great improvement of the lesions and of the itching. Omission of treatment in November resulted in a relapse within ten days. There was again rapid improvement when administration of the drug, 2 Gm. a day, was resumed, and a relapse followed when it was omitted in December 1939. Sulfanilamide medication was continued until March 1940, 1 to 2 Gm. a day. The drug was then changed to sulfapyridine, which was given in an amount of 1.5 Gm. a day for one year. From April 1941 to November 1941 no treatment was given, as there were only a few lesions. Since November 1941 the patient has again been taking sulfapyridine, 1 to 1.5 Gm. a day. There have never been any toxic symptoms.

CASE 9.—C. P., a woman aged 22, of Greek descent, had had dermatitis herpetiformis since the age of 8 years. The administration of sulfapyridine, 3 Gm. a day, was started in September 1941. Improvement began within a few days. On the ninth day of treatment the patient became nauseated. Treatment was therefore stopped. A few weeks later, after a dose of 0.5 Gm. of sulfapyridine the patient had severe nausea, which lasted for two days. No treatment with sulfonamide compounds was attempted from October 1941 to April 1942. She was then given 0.5 Gm. of sulfapyridine a day, and the dose was increased to 1 Gm. a day. This dosage was tolerated and also checked the disease.

Other Cases.—The remaining 4 cases did not show any striking deviation from those already described and are therefore not reported individually. No toxic symptoms from the drug were noted in these cases.

SUMMARY AND CONCLUSIONS

Intradermal tests with various bacterial vaccines were carried out on 12 patients with dermatitis herpetiformis. In 5 patients vesicular reactions were obtained following injections of Bact. coli vaccines. In 1 of the 5 patients a vesicular reaction followed also injections of staphylococcus vaccines; in another, administration of streptococcus vaccines. The vesicular response is probably based on bacterial allergy, but the allergy is not restricted to one particular bacterium.

Chemical studies of the blood were carried out for 15 patients. All values were within the normal range, with the exception of the sodium content of the serum, which was found to be slightly elevated in 4 of 11 patients.

During the past two and one-half years 13 patients with dermatitis herpetiformis have been treated with various sulfonamide compounds at the dermatologic clinic of the Massachusetts General Hospital.

Sulfapyridine was found to be effective in controlling the eruption of dermatitis herpetiformis. Its effect was, however, only temporary, and in order to maintain the improvement the administration had to be continued. The advisability of continued treatment over a long period is yet to be determined.

Sulfanilamide was found to be less effective than sulfapyridine, even when larger doses were given. Sulfathiazole proved to be of little value. Sulfaguanidine and sulfadiazine did not have any influence on the course of the disease.

All 13 patients were followed for a period of ten months or longer. Two patients were under continuous treatment for more than two years. Two patients had a toxic eruption from sulfanilamide. Nausea was caused in 1 patient by sulfanilamide and in another by sulfapyridine. No damage to the hemopoietic system was observed in any of the patients.

371 Commonwealth Avenue.

270 Commonwealth Avenue.

Clinical Notes

LYMPHOGRANULOMA VENEREUM OF UNUSUAL LOCATION AND EXTENT

Report of a Case

OSWALDO G. COSTA, M.D., Assistant in the Clinic of Syphilis and Cutaneous Diseases of the Faculty of Medicine, University of Minas Geraes, Bello Horizonte, Brazil.

The favorite site of lymphogranuloma venereum is the inguinoiliac lymph nodes. The unusual site and extent of the disease in my case are the reasons for reporting it. Costello and De Oreo also reported a case in which the lymphatic glands of the buttock and adjacent regions were involved.[1]

Lymphogranuloma venereum of unusual location and extent.

REPORT OF CASE

A. P. S., a Brazilian Negro aged 36, married, a clerk by occupation, resided at Contria, Minas Geraes. Both of his parents were dead, the cause of their death being unknown to the patient. Of four brothers and sisters who were living, one was epileptic, and the others were in good health. He had suffered from gonorrhea.

1. Costello, M. J., and De Oreo, G.: Lymphogranuloma Venereum: Report of an Unusual Example Involving the Lymphatic Glands of the Buttock and Adjacent Regions, Arch. Dermat. & Syph. **43**:997 (June) 1941.

The patient said that four years ago he had suffered from a small shallow soft ulcer in the sulcus of the penis. The ulcer disappeared spontaneously at the end of ten days. Thirty days after the disappearance of the penile lesion he noticed swellings in both inguinal regions, since which time the disease has attained its present development.

The patient had general malaise and weakness and had lost 17 pounds (7.7 Kg.) in weight. He presented stigmas of congenital syphilis, including Hutchinson teeth and saddle nose. A general examination of various systems and organs, including the spleen, gave otherwise normal results.

Dermatologic examination showed a small scar in the sulcus of the penis, which was apparently the remains of a lymphogranulomatous initial lesion. In the right inguinal region there were enlarged lymph nodes, some of which presented fistulas from which viscous pus was oozing. The lymph nodes were adherent to the skin, which was purplish. The intra-abdominal iliac nodes were perceptible on deep palpation. In the left inguinal region the lesions were similar to those on the right side, except that they were more extensive. They involved the crural region and the subcutaneous abdominal lymphatic vessels of the left side of the abdomen as high up as the umbilicus. The patient had never received proper treatment for lymphogranuloma venereum, as he had never consulted a physician.

The reaction to a Frei test was strongly positive, and the Kahn reaction of the blood was positive. The results of quantitative tests with tuberculin in dilutions of 1 : 1,000 up to 1 : 1,000,000 were all negative at the end of forty-eight hours.

Rua Ceará 1695.

REACTION DUE TO SULFAPYRIDINE IN THE TREATMENT OF DERMATITIS HERPETIFORMIS

JOHN F. MADDEN, M.D., ST. PAUL

The following case is cited to show that although sulfapyridine is an effective drug in the treatment of dermatitis herpetiformis, it may also be a dangerous one.

REPORT OF A CASE

Mrs. A. K., a white woman aged 40, a housewife, stated that a generalized eruption appeared about Nov. 1, 1942. The patient was seen at the dermatologic clinic of Ancker Hospital on December 1. She showed a generalized eruption which was most profuse on the trunk, upper extremities, face and anterior surfaces of the knees. The lesions were tense pinpoint-sized to pea-sized vesicles and wheals. Some were grouped and some were excoriated. Residual pigmentation remained at the sites of healed lesions. The patient was seen by the staff of the department of dermatology at the University of Minnesota on December 17, and all agreed with the diagnosis of dermatitis herpetiformis. The patient had not taken any medication and had not suffered from a previous eruption. She was given 7½ grains (0.5 Gm.) of sulfapyridine four times a day by mouth for two weeks. The eruption had practically disappeared except for residual pigmentation at the end of the first week. She continued to take the medicine until the end of the second week, when she was advised to reduce the amount of sulfapyridine to 7½ grains a day. The single dose of 7½ grains was followed by edema of the

lips, hands and feet. The patient discontinued taking the drug for two days and on the third day took two 7½ grain tablets of sulfapyridine. On the following morning there were superficial ulceration of the buccal mucosa, pharynx and palate and extensive edema of the extremities. The skin of the hands and feet was a deep violaceous color. Papular and iris type lesions appeared on the arms and legs. The patient's temperature was 99.6 F., and she complained of nausea and epigastric distress. The urine showed traces of albumin. The administration of sulfapyridine was discontinued, and the erythema-multiforme-like eruption disappeared in about a week. As the drug eruption receded, the lesions of dermatitis herpetiformis recurred.

COMMENT

It is my opinion that sulfapyridine should be given in the treatment of dermatitis herpetiformis only when the patient can be observed regularly and at short intervals.

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Correspondence

CONTACT DERMATITIS DUE TO RESIN-FINISHED FACING IN COTTON UNDERWEAR

To the Editor:—There is an article entitled "Contact Dermatitis Due to Resin-Finished Facing in Cotton Underwear," by Dr. Harry Keil, in the February 1943 issue (ARCH. DERMAT. & SYPH. **47**:242, 1943). In the introductory paragraph, the author thus explains the fact that the lengthy article was written on observations in 1 case: "This instance was deemed worthy of a separate report because the data collected shed light on the precise cause of the eruption, its pathogenesis and other related phenomena." It is seldom that I go out of my way to criticize the overestimation that an author makes of the worth of his article, but as the subject of dermatitis from fabric finishes was first brought to the attention of dermatologists by my studies and as I have a continuing interest in the subject, I wish to make the following comments on the article in question.

1. The author does not describe the garment. One can only infer that it was a white knit cotton union suit containing no admixture of wool.

2. He does not describe the "facing" or its location and purpose. I know that it is usually of white woven material, sewed on the inner surface of the knit fabric, to give support for buttons and buttonholes.

3. In paragraph 5, page 242, he states that on discovering the "facing" he performed patch tests with, among other things, various compounds of abietic acid, "wood rosin, one an FF grade and the other rich in phenolic bodies" (an unscientific statement. He should have given the designated grade as he did of the first one) and "methyl abietate 50 per cent by volume in xylene." In the same paragraph he states that he obtained a 1 to 2 plus reaction from rosin FF grade and further on he writes: "The remaining patches, which elicited no reactions, consisted of . . . one specimen of wood rosin FF grade . . ."

4. He does not explain why he performed patch tests with these special chemicals before he ascertained the chemicals contained in the "facing." He must be unaware of the facts often published by me that there are many chemicals used in processing fabrics and that the "finishes" are only one class of chemicals that can cause dermatitis. Moreover, I have often stated and proved that there are many kinds of finishes on the market which may cause dermatitis in sensitized persons. The ester gums, or glycerin abietates, are only one class of these finishes, the class that caused most of the dermatitis in the recent outbreak of dermatitis from shorts, nylon hosiery, etc., which was reported by me and my fellow authors. There are "finishes" made of urea-formaldehyde resins, of glyptal resins, of melamine resins and many others, all capable of causing allergic dermatitis in some sensitized subjects. Therefore, the author of the article in question had no valid reason to apply the patches of the many chemicals which he names before making sure that they were on the fabric, especially since it is known that they are sensitizers, and if the patient had not before been in contact with them, there was a possibility that the patches might sensitize the patient to chemicals to which he was not sensitive before.

Then, again, patch tests were performed with solutions in which xylene was the solvent. Xylene is a fat solvent and primary skin irritant. Positive reactions are to be expected from it on any skin, if its fat solvent action is not completely buffered.

All the patch tests with methyl abietate were performed by the author with use of xylene as a solvent. Nowhere does he state that he used the methyl abietate alone. The xylene played a major role in eliciting the positive reactions obtained from patches of methyl abietate in xylene. The author should have performed

patch tests on "controls" in order to check his results. He should also have performed some tests with xylene alone, with xylene plus liquid petrolatum and with methyl abietate alone (if he was sure that methyl abietate was in the fabric of the facing).

5. In paragraph 2, page 243, the author states: "About two weeks later I obtained a sample of the resinous substance which caused the dermatitis." He fails to state anywhere how he knew this "resinous substance" was the cause of the dermatitis. He does not state that he traced the underwear to its manufacturer and learned from him the nature of the chemicals with which it was processed (a difficult matter and one worthy of recording, if it was done) or whether he had a chemist determine it for him or whether he did it himself. Neither did he say that after these things were done, if they were done, he again performed patch tests on the patient with the chemicals with which the fabric was processed and found that "the resinous substance" was the actual cause and that the "resinous substance" was then found to be methyl abietate or that the manufacturer informed him that it was methyl abietate. He should have recovered the finish from the "facing" in the manner described by Schwartz and Tulipan (Schwartz, L., and Tulipan, L.: A Text-Book of Occupational Diseases of the Skin, Philadelphia, Lea & Febiger, 1939, p. 226) and performed patch tests with it and then given it to a chemist for identification. Failure to do these things refutes the claim of the author that "the data collected shed light on the precise cause of the eruption . . ."

6. In paragraph 3, page 243, the author states: "There were no constitutional symptoms and no exacerbations at the sites of other patches or in the original eruption itself . . ." This tends to show that the substance which actually caused the eruption was not applied to the patient's skin in a patch test. While it does not always happen, yet in many cases, especially when the patient is as sensitive as the one described seems to have been (required hospitalization), the application of the causative agent in a patch test relights the original dermatitis.

7. The time that various patches were applied and the intervals between the applications of the various series of patches are not stated. These are all-important factors in evaluating the results of patch tests.

8. The remaining five pages of the paper, devoted to "comment," can mean little as far as this particular case is concerned, when one considers the fact that the author has not proved that he found the actual cause of the dermatitis.

LOUIS SCHWARTZ, M.D., Bethesda, Md.

News and Comment

VENEREAL DISEASES DURING THE WAR

In his report as executive director of the American Social Hygiene Association, Dr. Walter Clarke stated that while the fight against venereal diseases is more effective in the present war than it was in the first World War it is not effective enough and the loss to the armed forces will be colossal unless civilians do their part much better. He referred to the intention of the federal government to build the armed forces up to 10,800,000 men and stated that if a venereal disease rate only one-half that of the first World War is achieved about 378,000 of these men will acquire syphilis or gonorrhea each year; that if the infected men lose on the average only one-half the time lost by first World War victims, the loss will total 7,560,000 man days per year and that this figure is equivalent to 21,000 men out of service and a burden to the medical facilities of the armed forces for one full year.

Dr. Clarke further stated: "Where will these 378,000 men become infected? Every one of them will be infected in civilian communities which allow prostitutes and promiscuous women and girls to spread disease to soldiers, sailors, marines and coast guardsmen. It is perfectly possible to prevent a large part of this waste if civilian communities will use the scientific weapons—legal, medical, social and educational—which are available.

"A smoothly operating national team composed of the Army, Navy, Public Health Service, Social Protection Section of the Federal Security Agency and American Social Hygiene Association is working day and night on this vital problem of war manpower. The work of the association, which is a participant in the National War Fund, is illustrated by the 1942 annual report released by the association today."

The report warns that the prostitution interests and the racketeers are not yet defeated and that the fight begun so successfully is not yet won. The report of the association calls for expanded activities, constant vigilance and increased vigor during 1943 as the armed forces of the United States grow and its war industries approach peak production.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

POST-VACCINAL MENINGO-ENCEPHALO-MYELITIS. T. M. DUNN and R. H. RIGDON, Am. J. Clin. Path. **11**:771 (Oct.) 1941.

In a case of postvaccinal encephalitis Dunn and Rigdon obtained a 4 plus Wassermann reaction of the blood and a 3 plus reaction of the spinal fluid. The pathologic changes were identical with those previously described in cases of postvaccinal encephalitis, and the patient was only 16 years of age. These points suggest that the reactions were falsely positive, as in the case of positive serologic reactions in the blood of a vaccinated person.

A NOTE ON THE DEVELOPMENT OF CUTANEOUS ARTERIAL "SPIDERS" and PALMAR ERYTHEMIA IN PERSONS WITH LIVER DISEASE AND THEIR DEVELOPMENT FOLLOWING THE ADMINISTRATION OF ESTROGENS. WILLIAM BENNETT BEAN, Am. J. M. Sc. **204**:251 (Aug.) 1942.

Bean studied cutaneous arterial "spiders" in 359 persons with hepatic disease, pregnancy or nutritional disorders and was impressed with the possibility of the relationship of these lesions to abnormal metabolism of certain 17-keto steroid hormones, particularly the estrogenic substances. The chief reasons for Bean's assumption were: the knowledge that hepatic disease interferes with 17-keto steroid metabolism, the appearance of "spiders" in pregnancy at the period when there is an increase in excretion of estrogens and the observation of visible changes in spiders during the menstrual cycle.

Three men who were chronically addicted to the use of alcohol were given diethylstilbestrol by mouth or alpha estradiol dipropionate intramuscularly. Cutaneous arterial spiders developed in 2 and palmar erythema in 1.

EFFECT OF LARGE AMOUNTS OF SINGLE VITAMINS OF THE B GROUP UPON RATS DEFICIENT IN OTHER VITAMINS. KLAUS UNNA and JOSEPHINE D. CLARK, Am. J. M. Sc. **204**:364 (Sept.) 1942.

Previous observers have noted that diets deficient in several members of the vitamin E complex may cause deficiency diseases in which lesions characteristic of the lack of the various single factors might not become conspicuous, and it is generally accepted that the characteristic lesions due to a deficiency in one single factor are more rapidly produced on diets which supply an optimum amount of all other factors.

Unna and Clark studied rats maintained on highly purified diets free from riboflavin, pyridoxine, pantothenic acid or the entire B complex and on diets partially deficient in riboflavin or pantothenic acid. These rats were then fed large amounts of single crystalline vitamins of the B group, but the manifestations of the deficiency state were not aggravated.

LYNCH, St. Paul.

INTERSTITIAL KERATITIS: ANALYSIS OF FIVE HUNDRED AND THIRTY-TWO CASES WITH PARTICULAR REFERENCE TO STANDARDIZATION OF TREATMENT. J. V. KLAUDER and ELEANOR VANDOREN, Arch. Ophth. **26**:408 (Sept.) 1941.

This study was concerned with the evaluation of various forms of treatment in terms of visual acuity of the patients at the final examination. Vision as corrected by glasses was not always recorded, either because it was so good that refraction was not necessary or because it was so poor that glasses did not help.

Ninety-seven per cent of the patients were treated with arsenicals and bismuth or mercury. Iodides, fever therapy and local heat were employed.

While treatment instituted during the inactive stage did not improve vision, routine continuous treatment with arsenicals and a heavy metal gave superior visual results; the administration of iodides unfavorably influenced final visual acuity.

WESCOTT, Chicago [Am. J. Dis. Child.].

THE CONCEPT OF ATOPY IN THE LIGHT OF RECENT INVESTIGATIONS. ERICH URBACH, Arch. Pediat. **58**:482 (Aug.) 1941.

The reasons commonly advanced as the basis for the segregation of "atopies" from experimental anaphylaxis are reviewed in the light of recent investigations. The distinctions between them, previously emphasized as fundamental, are shown to depend on extrinsic factors, such as modes, routes and intensity of sensitization.

While "atopic reagins" differ serologically from the anaphylactic antibodies to some extent, they are immunologically closely related and perhaps even identical, as shown by the successful passive transfer of human "atopies" to lower animals and of animal anaphylaxis to man.

The theory that hypersensitiveness in man and experimental anaphylaxis are only different expressions of a single underlying biologic process dependent on a cellular antigen-antibody mechanism is supported by numerous experimental and clinical observations.

PROGNOSIS IN ERYTHEMA ANNULARE RHEUMATICUM. MARVIN GRUBMAN, Arch. Pediat. **58**:521 (Aug.) 1941.

Grubman reports 1 case of erythema annulare rheumaticum which was associated with a mild rheumatic infection and minimal cardiac abnormalities. The eruption has lasted, with only short remissions for over two years.

ORR, Buffalo [Am. J. Dis. Child.].

TREATMENT OF DEMENTIA PARALYTICA: A FIVE YEAR COMPARATIVE STUDY OF ARTIFICIAL FEVER THERAPY AND THERAPEUTIC MALARIA IN TWO HUNDRED AND THIRTY-TWO CASES. J. R. EWALT and F. G. EBAUGH, J. A. M. A. **116**:2474 (May 31) 1941.

Ewalt and Ebaugh report a comparative study of the relative effectiveness of malaria and of artificial fever therapy. During five years one of these therapeutic methods was used in the treatment of *232* patients, the patients being alternated in sequence. The results showed that of the patients treated with artificial fever 69 per cent had either remissions or improvement, while in the group treated by malaria therapy 58 per cent obtained improvement. The authors favor artificial fever therapy not only because of the superior results but also because it is safer, may be used with patients in whom malaria is contraindicated and may be combined with the administration of antisyphilitic drugs.

URTICARIA DUE TO ALIPHATIC ALDEHYDES: A CLINICAL AND EXPERIMENTAL STUDY. B. Z. RAPPORT and M. M. HOFFMAN, J. A. M. A. **116**:2656 (June 14) 1941.

In a patient who had frequent attacks of urticaria for fifteen months, the cause was shown to be sensitivity to aliphatic aldehydes. The substances which caused the symptoms were formaldehyde, with which he came in contact in his work, and acrolein, a combustion product of glycerin inhaled in cigaret smoke and also ingested with shallow-fried or broiled foods. The patient smoked cigarets in which the hygroscopic agent was diethylene glycol instead of glycerin, and the hives disappeared. The lesions reappeared when a small amount of glycerin was introduced with a toothpick into the cigaret. The authors point out that many foods and commonly used essential oils contain aliphatic aldehydes.

ROENTGENOGRAPHIC DIAGNOSIS OF CONGENITAL SYPHILIS IN UNERUPTED PERMANENT TEETH. B. G. SARNAT, I. SCHOUR and R. HEUPEL, J. A. M. A. **116**:2745 (June 21) 1941.

Sarnat, Schour and Heupel report the roentgenologic diagnosis of congenital syphilis based on the unerupted permanent central incisors and first molars of a child aged 4 years. This was confirmed two years later, when the teeth had erupted. According to the authors this method of diagnosis of congenital syphilis should be used in conjunction with roentgen study of the long bones.

RECURRENT SCARRING PAINFUL APHTHAE: AMELIORATION WITH SULFATHIAZOLE IN TWO CASES. R. L. SUTTON, J. A. M. A. **117**:175 (July 19) 1941.

Sutton reports the histories of 2 patients suffering from periadenitis mucosa necrotica recurrens. Both patients were temporarily relieved from the painful lesions following sulfathiazole therapy. This treatment did not prevent new lesions from appearing several weeks after discontinuance of the therapy.

THE CONFUSING MULTIPLICITY OF SEROLOGIC TESTS FOR SYPHILIS: STANARDIZATION OF THE SEROLOGIC REPORT AS A POSSIBLE SOLUTION. J. E. MOORE and H. EAGLE, J. A. M. A. **117**:243 (July 26) 1941.

Because of the increased variety of serologic tests for the diagnosis of syphilis with the frequent conflicting results, Moore and Eagle suggest that the reporting laboratory should interpret the results and give a composite report of positive, doubtful or negative. The onus of interpreting conflicting laboratory results is thus placed on the person best qualified, the laboratory director.

ROCKY MOUNTAIN SPOTTED FEVER. J. G. Hutton, J. A. M. A. **117**:413 (Aug. 9) 1941.

Hutton reports the histories of 3 patients with Rocky Mountain spotted fever. Two recovered, and 1 died. He states that the fatality rate has been shown to be 19.4 per cent in the Western states and 18.1 per cent in the South Atlantic states. The disease has been observed in thirty-seven states. Because of the possibility of confusion in diagnosis with typhus fever or with other cutaneous diseases, a confirmatory test is desirable to support the clinical diagnosis in every suspected case. The three tests ordinarily used are the infection test, the Weil-Felix reaction and the protection, or virus neutralization, test. There is no specific treatment. According to Hutton, vaccine prepared by the United States Public Health Service protects fully against the less virulent strains and partially against the highly fatal type of Rocky Mountain spotted fever, the protection being retained for less than a year.

FALSE POSITIVE SEROLOGIC REACTIONS FOR SYPHILIS DUE TO SMALLPOX VACCINATIONS (VACCINIA). F. W. LYNCH, R. E. BOYNTON and A. C. KIMBALL, J. A. M. A. **117**:591 (Aug. 23) 1941.

Lynch, Boynton and Kimball studied the effect of primary vaccinia on the results of serologic tests for syphilis. Of the 263 persons who gave no reactions before vaccination, 43 (16 per cent) reacted to one or more of four standard serologic procedures and 23 (9 per cent) reacted to more than one type of test. Most of the positive reactions were weak but a few were strong. The reactions remained positive for several weeks or even months.

CANCER OF THE LOWER LIP: TREATMENT WITH RADIATION. J. H. LAMB and W. E. EASTLAND, J. A. M. A. **117**:600 (Aug. 23) 1941.

Lamb and Eastland report on the result of treatment of 318 patients with cancer of the lower lip. They report a 72.2 per cent five year survival rate. The technic

of treatment has changed with experience from the use of unfiltered roentgen radiation and beta radium radiation to more heavily filtered and longer doses of these physical modalities.

DEVELOPMENT OF ACUTE EXFOLIATIVE DERMATITIS DURING ADMINISTRATION OF SULFATHIAZOLE. M. WEINSTEIN and A. H. DOMM, J. A. M. A. **117**:607 (Aug. 23) 1941.

A Negro aged 38 received in less than two days a total of 15 Gm. of sulfathiazole, free of phenobarbital, for the treatment of an atypical pneumonia. A diffuse macular rash was then noted. Although administration of the drug was ordered discontinued, an additional 4 Gm. was given the patient. The rash became vesicular and later almost universally exfoliative. The rash was accompanied by fever and toxemia. Death occurred seven days after the first dose of the drug was administered. An autopsy failed to disclose anything significant, and death was assumed to be due to an overwhelming toxemia. It is of significance that the patient experienced a cutaneous reaction in 1929 following intravenous injections of arsphenamine.

LEWIS, New York.

A METHOD FOR THE EVALUATION OF WATER SOLUBLE AND WATER MISCIBLE FUNGICIDES USED IN THE PREVENTION OF THE SPREAD OF "ATHLETE'S FOOT." E. G. KLARMANN, V. A. SHTERNOV and S. M. COSTIGAN, J. Bact. **42**:225 (Aug.) 1941.

In their summary the authors state that this paper describes a method for the evaluation of the fungicidal action of water-soluble or water-miscible preparations intended particularly for prophylactic purpose and for application to inanimate objects. Trichophyton rosaceum is used as the test organism. For the sake of uniformity of routine bacteriologic testing technic, the operating procedure has been patterned along the lines of the Food and Drug Administration's method of testing disinfectants.

STOESSER, Minneapolis [Am. J. Dis. Child.].

ETIOLOGY AND TREATMENT OF URTICARIA: DIAGNOSIS, PREVENTION AND TREATMENT OF POISON-IVY DERMATITIS. PERRY C. BAIRD JR., New England J. Med. **224**:649 (April 10) 1941.

Urticaria.—According to Baird, urticaria should be thought of not as a disease manifesting itself solely in the skin but as a process capable of involving many other structures and organs of the body, such as the stomach and the throat or larynx. On theoretic grounds, urticaria might extend to the lungs, producing a form of pulmonary edema; to the heart, producing paroxysmal tachycardia; to the brain, causing headaches; to the bladder, creating hematuria, and then to the urethra, causing anuria.

It seems true, as indicated by Sulzberger and Goodman, that some types of urticaria are definitely not allergic. In Urbach's review of 500 cases of urticaria, he noted that only 20 per cent could be interpreted as instances of allergy. The allergic types of urticaria and angioneurotic edema are common and represent in all probability a true antigen-antibody relation in cases of pollen sensitivity, serum disease and reactions to foreign protein. It is possible that urticaria-producing drugs, such as acetylsalicylic acid, may combine with body proteins and become allergenic.

On the basis of clinical experience, it is natural to divide urticaria into acute and chronic types. The acute form usually runs a brief course, lasting from a few days to two or three weeks, and terminates as a rule in complete recovery. The chronic condition has lasted for months or years. Cutaneous tests in urticaria are of decidedly limited value.

In the search for the cause of acute urticarial recurrences, the patient's own observations regarding causative agents are of the greatest value. Frequent causes are foods, inhalants and contactants. Foci of infection represent a common cause

of chronic urticaria. Nervous and emotional stress and strain can without any doubt elicit urticarial attacks. Urticaria occasionally may be caused by acrolein formed by the oxidation of fat, as in frying or broiling or in smoking cigarets moistened with glycerin. Acrolein is related to formaldehyde, which also may cause urticaria. Many other unusual causes are reported in this article, as well as many unusual forms of treatment.

Treatment: The circulating allergens that produce acute hives are, with scarcely any doubt, usually of alimentary origin. Therefore, the first step in etiologic therapy is to clean out the gastrointestinal tract. The food should be bland and the intake limited. Fluids should be forced to aid elimination of allergens. Violent exercise should be avoided, because it increases the blood supply to the skin and increases the severity of symptoms. The relief of intolerable crises of itching is often best accomplished by application of heat, such as immersion of the part in water as hot as the skin will bear.

Poison Ivy Dermatitis.—Of all the cutaneous eruptions caused by plant substances, that produced by the different species of Rhus is probably the commonest in North America. Shelmire's experiments indicate that the dermatitis-producing principle of poison ivy is not an oil, as previously described, but a dialyzable fraction of the oleoresin soluble in water and in urine.

An acute dermatitis presenting clearcut vesicles, with or without bullae, appearing suddenly on exposed regions of the body should always arouse suspicion of dermatitis venenata. Internal manifestations of poison ivy poisoning may occur. The majority of such eruptions have been caused by chewing the leaves or by swallowing the juice to obtain immunity. One of these terminated fatally (Alumbaugh).

Prophylaxis and Treatment: Protection against poison ivy dermatitis may be afforded by application of an oxidizing agent to the skin prior to deliberate exposure to the plant. Potassium permanganate solution (0.1 per cent) and ferric chloride solution (3 to 5 per cent) have been found to be useful. Also a preparation containing 10 per cent sodium perborate incorporated in a base of vanishing cream has been effective.

No type of topical application has any consistently dramatic effect in the treatment of poison ivy dermatitis. The dramatic results from therapy have seemed to come mostly from the use of poison ivy extracts given by intramuscular injection.

Topical applications of value in the treatment of poison ivy dermatitis include the following: potassium permanganate solution (0.02 per cent), boric acid solution (2 per cent), solution of aluminum acetate (Burow's solution) (diluted 1:16) and phenolized zinc oxide lotions.

Opinions regarding value of the injections for therapy and prophylaxis of poison ivy dermatitis are widely divergent. Roentgen therapy is useful and is often employed for severe and stubborn eruptions. It is effective in doses so small as to involve no hazard whatsoever.

GENGENBACH, Denver [Am. J. Dis. Child.].

EXFOLIATIVE DERMATITIS (RITTER'S DISEASE) TREATED WITH SULFATHIAZOLE. ADOLPH G. DESANCTIS and F. C. DELORENZO, New York State J. Med. **41**:1361 (July 1) 1941.

A boy of Jewish parentage 16 days of age was treated for exfoliative dermatitis (Ritter's disease) with sulfathiazole. Within two days marked improvement was shown. Diarrhea developed, however. This stopped when use of the drug was discontinued. The infant was discharged in ten days, having gained 10 ounces (283 Gm.) in weight.

AIKMAN, Rochester, N. Y. [Am. J. Dis. Child.].

ECZEMA IN INFANCY AND CHILDHOOD. K. BAIN, South. M. J. **34**:863 (Aug.) 1941.

Bain reports on 168 cases of eczema in infancy and childhood which were encountered in a five year period. Twenty-two and four-tenths per cent (22.4 per

cent) of the patients were on breast feeding alone when eczema developed. Milk is the most common single offender in causing the condition, and its elimination from the diet offers the greatest chance for cure.

MULTIPLE HEREDITARY HEMORRHAGIC TELANGIECTASIA. W. E. STOREY, South. M. J. **34**:934 (Sept.) 1941.

Storey reports on a case of multiple hereditary hemorrhagic telangiectasia.

Hematoxylin-eosin-stained sections of a typical telangiectatic area indicate that there is no pronounced difference in visible histologic structure from that of a simple nevus. It is suggested that bleeding, especially when spontaneous, may be more dependent on other factors than visible histologic lesions.

With rare exceptions, local measures do not appear to yield anything but the most temporary benefit.

The author believes that the subcutaneous injection of moccasin venom (Ancistrodon piscivorus) offers some promise as an effective therapeutic measure.

SCHLUTZ, Chicago [Am. J. Dis. Child.].

THE MANAGEMENT OF INFANTILE ALLERGIC ECZEMA. GERALD M. CLINE, Wisconsin M. J. **40**:789 (Sept.) 1941.

The need for a careful history with emphasis on the possible relation of food additions to the eruption are pointed out. Since the use of superheated milks in recent years, the violent eczemas of former years are rare. In the feeding of children with allergic eczemas, if these milks do not relieve them, goat's milk or a milk substitute (soybean, etc.) may be used. Such changes have in the tests of the author relieved about 50 per cent of his patients. When food restrictions are made, adequate vitamins and minerals, especially calcium, must be added. The dangers of anaphylactic reactions when the child is again given a previously used food are pointed out. For addition of sugar he prefers sucrose and believes that corn syrup (glucose) must be used with caution. Crystalline vitamin D_2 (calciferol), carotene and crystalline vitamin C (ascorbic acid) are substituted for ordinary forms of vitamins D, A and C. Rice is believed the least allergenic cereal. Eggs and tomatoes are most frequent offenders, while potatoes, spinach, string beans and commercially mixed greens are to be avoided.

Cutaneous testing in infantile eczema is unsatisfactory. Passive transfer testing may be helpful. Possible environmental allergens must be eliminated. Wool, feathers, glue, rubber, soap, paints, varnishes, dyes, cottonseed and kapok may be important. Scratching and traumatizing the skin must be controlled. Local applications must be individualized and varied with the progress of the patient.

JANNEY, Wauwatosa, Wis. [Am. J. Dis. Child.].

DERMATITIS VENENATA PROVOKED BY COLEOPTERA GENUS PAEDERUS. PEDRO L. BALIÑA, Rev. argent. de dermatosif. **23**:522, 1939.

In 1915 the author described a dermatitis due to an insect. Later investigations of Baccaredda in Italy and Dallas in Argentina have identified Paederus fuscipes as the cause of this dermatitis. The condition is frequent in the summer. It begins twenty-four to forty-eight hours after the contact of the insect with the skin. First there is an intense pruritus. Later vesiculation appears. The eruption is self limited and disappears in five to eight days except when secondarily infected. The dermatitis is produced by the crushing of the insect against the skin. A yellow fluid is thus liberated, which stains the skin and produces a burning sensation. This substance if carried to the eyes with the fingers may produce conjunctivitis. The patch of dermatitis is usually 2 to 3 inches (5 to 7.5 cm.) in diameter, and in some instances a linear lesion was noticed, simulating herpes zoster or dermatitis venenata due to plants. The latter type of lesion was probably due to

unconsciously rubbing the insect against the skin. The eruption is located usually on uncovered parts of the body, face, neck and hands. Paederus is found in some regions of Argentina, Brazil and Ecuador.

HISTOPATHOGENESIS OF LYMPHOGRANULOMA VENEREUM. WALDEMAR E. COULTS, I. BRIEVA, J. LENER and A. SAID, Rev. argent. de dermatosif. **26**:167, 1942.

The authors review the studies made on the virus of lymphogranuloma venereum. After many experimental studies made at the Department of Health of Santiago, Chile, they conclude that the inclusions are frequently seen in the tissues of lymphogranuloma venereum. They occur in the cytoplasm and are basophilic. They may be small (less than 1 micron) or large (5 to 20 microns). The former are usually seen in the early lesions and the latter in the late stages. The inclusions may live and multiply in the brain tissue of inoculated guinea pigs and rabbits, producing a meningoencephalitis. The inclusions may be cultured in chick embryos.

In women without clinical lesions of lymphogranuloma venereum inclusions were found in vaginal cells. These inclusions inoculated in chick embryos gave positive results. This fact suggests that there may be carriers of the infection.

CAÑIZARES, New York.

Society Transactions

MINNESOTA DERMATOLOGICAL SOCIETY

F. W. LYNCH, M.D., *President*

H. A. CUMMING, M.D., *Secretary*

Duluth, July 1942

Epithelioma. Presented by DR. E. Z. SHAPIRO, Duluth.

Mrs. L., a white woman aged 67, five years ago had a small typical epithelioma on the left temple. The first treatment applied was a 10 mg. plaque of radium. Sixty milligram hours was given. Three years later the lesion was much the same, but larger, and a second dose of the radium treatment was given, but this also was unsuccessful. Plastic surgery was suggested, but because of the poor general health of the patient this could not be done. The lesion has grown rapidly, until it is now 2 inches (5 cm.) in diameter and the malignancy involves the frontal bone, which is exposed in several areas. Roentgen therapy of high voltage was used at St. Mary's Hospital, and the lesion itself cleared about 95 per cent.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: I believe that this lesion could well be handled by surgical means. I recently had a patient with an epithelioma in the same area, and a good cosmetic and therapeutic result was obtained by surgical methods. I think dermatologists sometimes attempt to hold patients with such lesions too long with dermatologic therapy.

DR. E. Z. SHAPIRO, Duluth: In a discussion with Dr. Murphy of Chicago regarding the use of roentgen therapy of high voltage for recurrent epitheliomas in this area, I learned that he had produced many clinical cures. In the case presented today this therapy was tried, but the result was not entirely satisfactory. Because of this patient's age and existing nephritis, surgical procedures are rather hazardous.

A Case for Diagnosis (Onycholysis?). Presented by DR. F. T. BECKER, Duluth.

R. M., a white woman aged 21, first had difficulty with her toe nails and finger nails after an attack of pneumonia in 1939. Since that time her nails have become dark and four or five of them have become loose at their bases and have been shed.

Her nails are dirty gray and somewhat thickened in the center. Several are loose and can be pushed back like a door on a hinge.

Onycholysis. Presented by DR. GEORGE DOYLE, Duluth.

Mrs. M. D., a white woman aged 60, first noticed a separation of her right middle finger nail in June 1941. Soon afterward she noticed similar changes in her left middle finger nail.

In August 1941 she began to have cramps in the muscles of her right foot, and later cramps developed in her left foot. They sometimes involve the muscles of her calf. She has had typical attacks of tetany.

A routine physical examination in August 1941 showed no abnormalities except a low value for calcium and for phosphorus in the blood.

She was given large doses of calcium gluconate by mouth with decided improvement of the symptoms, although she still has mild attacks of tetany. The separation of her nails has remained the same. The calcium content of the blood and the blood count in December 1941 were normal.

A diagnosis of onycholysis associated with low calcium content of the blood and tetany was made.

DISCUSSION OF CASES OF ONYCHOLYSIS

DR. E. M. RUSTEN, Minneapolis: I have seen patients with onycholysis, and there were equal numbers who had used nail polish and who had not, and who had done housework and who had not. I believe that the improvement was rather spontaneous and that no type of treatment had any therapeutic value.

DR. F. W. LYNCH, St. Paul: I wish that more cases of this kind could be presented before the society. I wonder if any one has received good results from the administration of calcium and thyroid.

DR. E. C. GAGER, St. Paul: I distinctly remember such a case in which there was an indicated calcium deficiency and definite improvement with the administration of calcium.

DR. C. W. LAYMON, Minneapolis: Dr. Howard Fox has found that a patient with a low basal metabolic rate is greatly helped by the administration of thyroid and that a change of occupation and protection of the nails are essential therapeutic measures.

Sarcoid. Presented by DR. E. Z. SHAPIRO, Duluth.

Mrs. K. has had a lesion on her left cheek just below the eye for one month. It appeared after she had rubbed her cheek with soapstone to remove some paint. When she was first seen there was a lump in this area, about a ¼ inch (0.6 cm.) in diameter. It was soft, boggy, raised above the level of the skin and dark bluish, without scaling. She was given roentgen treatment (800 r) for two weeks, and it seemed to have melted away. A month later it recurred and looked about the same as when first seen.

DISCUSSION

DR. L. H. WINER, Minneapolis: At present I do not think there is enough eruption present to indicate a diagnosis, but with the transitory phase of the eruption I suggest a diagnosis of a fixed drug eruption.

DR. H. E. MICHELSON, Minneapolis: How was the diagnosis arrived at? Was a biopsy performed?

DR. E. Z. SHAPIRO, Duluth: The diagnosis was entirely clinical.

Erythema Induratum. Presented by DR. E. Z. SHAPIRO, Duluth.

Miss E. W., a white woman aged 23, for three months has had a lesion measuring 1 by 3 inches (2.5 by 7.5 cm.) on the outer surface of the left leg, on the midportion down near the ankle. The area is red, raw and oozing. The ulcer is sharply demarcated, and there are small new ulcers starting on the circumference of the large one. There also seems to be some blue discoloration. The Wassermann reaction was negative but the Mantoux reaction strongly positive. This woman had previously been a patient at Nopeming Sanatorium, Nopeming, Minn., and had had a bilateral salpingectomy for tuberculosis of the fallopian tubes, following which there was a long history of a draining sinus.

DISCUSSION

DR. JOHN MADDEN, St. Paul: Because of the location of the lesion I believe it is more likely a pyoderma than a lesion of tuberculous origin.

DR. H. E. MICHELSON, Minneapolis: I think that this patient probably has an ecthyma; strapping the leg with adhesive tape might be a helpful therapeutic measure.

A Case for Diagnosis (Erythema Induratum?). Presented by DR. F. T. BECKER and DR. W. R. BAGLEY (by invitation), Duluth.

Mrs. C. R., a white woman aged 51, first had an ulcer on her left leg, which became progressively larger until the foot sloughed off just above the ankle. She stated that this procedure was not very painful and that the extremity was never blue or discolored. A physician was first consulted early in 1942, and an amputation of the leg was performed.

General physical examination reveals a slightly undernourished woman with these essential physical abnormalities: a perforated nasal septum and three or four draining sinuses about the rectum. On the right shin are several ulcerations about 2 cm. wide and 3 or 4 cm. long with a small amount of purulent exudate. There are also several bluish red walnut-sized subcutaneous nodules on both surfaces of the leg.

The reaction to a Mantoux test was positive with a dilution of 1 to 10,000. A roentgenogram of the lungs showed fibrotic areas in both apexes and bilateral calcified nodes. Examinations of nasal discharge and sputum showed no acid-fast bacilli; cultures of material from the ulcers showed staphylococci. The Kline test gave negative results in both blood and spinal fluid. The hemoglobin content was 81 per cent and the white blood cell count 6,100.

DISCUSSION

DR. E. M. RUSTEN, Minneapolis: There is a possibility of a self-induced eruption.

DR. L. H. WINER, Minneapolis: The microscopic sections showed an inflammatory reaction around the blood vessels with some endarteritis, such as would be seen in an embolic reaction.

DR. F. W. LYNCH, St. Paul: This patient has a perforated septum in which there is definitely no clinical or serologic evidence of syphilis; self-induced eruptions and also the perforation of the septum could be explained on this basis.

DR. H. E. MICHELSON, Minneapolis: It might be well to have this patient examined by a psychiatrist. There is the possibility that the patient may be inflicting this eruption on herself.

Lupus Erythematosus with Bilateral Tuberculous Keratitis. Presented by DR. E. Z. SHAPIRO, Duluth.

O. S., a 46 year old man, had lupus erythematosus of the face and ears, and a tuberculous keratitis developed, necessitating injections of old tuberculin. This produced good results in the cutaneous eruption as well as the keratitis. He received no other treatment for the lupus erythematosus. The man was given a check-up at Nopeming Sanatorium, Nopeming, Minn., and an old healed lesion was found in one lung. The ocular involvement is still active and painful.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: I think this man should have further consultation regarding his eyes, as he is rapidly losing his vision.

DR. F. W. LYNCH, St. Paul: Considerable improvement has been noted in patients with keratitis after the use of beta rays of radium.

Raynaud's Disease. Presented by DR. F. T. BECKER, Duluth.

Mrs. J. A., a white woman aged 30, has noticed pain and bluish discoloration of her toes for the past year. Since April 1942 the disease has become more severe; it also involves her finger tips and is aggravated by cold.

Examination of her skin when she was first seen, in May 1942, showed a severe cyanosis of all the toes, several of which were ulcerated at the periphery.

This has improved by local application of heat. Her fingers are cold and bluish red; when the hands are immersed in cold water the fingers become blue, swollen and painful.

The results of general physical examination were normal except for the cyanosis described. Her basal metabolic rate was + 16 per cent. A surgical consultant has advised sympathectomy.

DISCUSSION

DR. E. STRAKOSCH (by invitation), Minneapolis: Many investigators of Raynaud's disease have felt that it is definitely an allergy to cold and that sympathectomy only helps the pain and does not bring vascular improvement.

Lichen Planus. Presented by DR. E. Z. SHAPIRO, Duluth.

L. P., a man aged 60, has lichen planus of the mouth. Several years ago he also had lesions on other parts of his body. They cleared up with bismuth therapy and roentgentherapy, but there is still some evidence of the disease in his mouth.

Lichen Planus. Presented by DR. E. Z. SHAPIRO, Duluth.

Mr. H. N. has lesions on the back, legs and arms. The lesions consist of papules of various sizes, some with definite groupings and others scattered without any form. There is a very slight scaling over some of these lesions.

DISCUSSION OF CASES OF LICHEN PLANUS

Dr. H. E. MICHELSON, Minneapolis: Dr. Ormsby formerly favored the use of bismarsen, but after a thorough trial he found it was no more valuable than mercury bichloride.

DR. JOHN MADDEN, St. Paul: Five years ago I had a patient with generalized lichen planus who showed much improvement under long habituation with alcohol and who had a severe recurrence six months after he stopped drinking.

DR. C. W. LAYMON, Minneapolis: Dr. Oppenheim has always preferred arsenic in the treatment of lichen planus. Dr. Michelson used mercury for a long time, and others used bismuth, with apparently equal results. In a recent review by Lord of the various types of therapy, it was stated that there are recurrences usually in 15 to 20 per cent of the cases.

DR. H. E. MICHELSON, Minneapolis: Although recurrences are rather frequent, I believe therapy of some kind is necessary to produce any improvement.

DR. L. H. WINER, Minneapolis: Lichen planus of the lower extremities gives the most difficulty and is least responsive to treatment.

DR. H. E. MICHELSON, Minneapolis: I find that in the semiverrucous type of lichen planus on the lower extremities improvement is usually satisfactory when I use solid carbon dioxide.

DR. C. W. LAYMON, Minneapolis: Patients often complain of severe pain following the administration of mercury bichloride.

DR. H. E. MICHELSON, Minneapolis: I use a mercury bichloride solution containing 2 per cent phenol, which alleviates the pain.

DR. JOHN MADDEN, St. Paul: I have even had good results with the use of mercuric succinimide.

Necrobiosis Lipoidica Diabeticorum Without Diabetes. Presented by DR. E. Z. SHAPIRO, Duluth.

This woman was shown three years ago at a local meeting and is shown again at this time to observe the subsequent progress. As seen today, there are round and oval lesions on the left shin. They are smooth and shiny, and there

are numerous fine blood vessels showing underneath that disappear under diascopic pressure. There is also a yellowish brown pigmentation. The lesions are sharply demarcated from the surrounding skin.

DISCUSSION

DR. F. T. BECKER, Duluth: Dr. Oppenheim has stated that a patient with this disease is either diabetic or potentially diabetic. This patient should have a thorough study, especially a dextrose tolerance test.

HENRY E. MICHELSON, M.D., *President*

HARRY A. CUMMING, M.D., *Secretary*

Rochester, Oct. 11, 1942

Presentation of all cases at this meeting was made by Dr. Paul A. O'Leary, Dr. Hamilton Montgomery and Dr. Louis A. Brunsting, of Rochester.

Pemphigus Vegetans.

I. G., a Jew aged 49, reported Sept. 29, 1942 because of bullae in the mouth which appeared three months ago and which were followed by ulcerations. Recently bullae developed in the left nares, on the neck and chin and in the right axilla, many of which subsequently have become vegetating.

The general health is good. There has been a recent loss of weight, 5 to 7 pounds (2.3 to 3.2 Kg.), attributed to the sore mouth and throat with difficulty in swallowing. The results of laboratory tests were as follows: urine normal, hemoglobin 14.8 Gm., white blood cells 9,000, eosinophils 5.5 per cent and an otherwise normal differential count.

Treatment for the past ten days has consisted of intravenous injections of naphuride (an American brand of the compound that has been sold also as "germanin").

DISCUSSION

DR. RUBEN NOMLAND, Iowa City: I think occasionally one sees benign pemphigus limited to the mouth. In spite of the fact that cutaneous lesions have recently developed, I do not believe the prognosis is too bad. In the last three years I have seen 5 persons with blistering lesions in the mouth. Two eventually had cutaneous lesions and died of the pemphigus; the other 3 are doing well.

DR. HERBERT C. LEITER, Sioux City, Iowa: I have had an opportunity to follow 1 of the patients whom Dr. Nomland discussed, the one with pemphigus of the lower extremities who had been under treatment in Iowa City. Although the pemphigus was of five or six years' duration, the patient's general condition was good. Occasionally, there are lesions which heal readily without special treatment.

DR. OLIVER S. ORMSBY, Chicago: The subject of pemphigus is too extensive to discuss under the circumstances; so I shall make a few remarks about pemphigus vegetans. In my early experience I used to think that pemphigus vegetans and pemphigus foliaceus were 100 per cent fatal and that occasionally patients with pemphigus vulgaris and other types would recover. In the past few years the situation has changed considerably. I have had more patients with pemphigus vegetans recover than those with pemphigus vulgaris. For about three years I have been using acetarsone, recommended by Oppenheim, with good results, and the technic is as follows: The entire dose for any one day is dissolved in water or taken as a capsule followed by a glass of water thirty minutes before breakfast. The first three days 1 tablet (the standard tablet contains 0.25 Gm.) is given thirty minutes before breakfast. A rest period of three days follows, and if there has been no intolerance the next day 2 tablets are given before breakfast, the following

day 3 tablets and the third day 3 tablets. This is the maximum dose. It should be followed by three days' rest, three days' treatment, three days' rest, and so forth, until the number of tablets given equals the number of kilograms the patient weighs. In the treatment of pemphigus vegetans, acetarsone is a valuable preparation.

In regard to the lesions of the mouth, which Dr. Nomland spoke about, I have seen a number of patients who have had lesions of the mouth for two or three years before lesions on the skin developed. My experience indicates that lesions of the mouth are of serious portent.

I think pemphigus of the eye is another subject that is worth discussing briefly, because until three years ago I thought that ocular pemphigus as described by ophthalmologists was unrelated to cutaneous pemphigus. I have seen a large number of patients with pemphigus of the skin but none with lesions of the eye; however, in the last two or three years I have seen several in whom there was a definite connection. Pemphigus of the eye is terribly deforming as far as the eye is concerned, although in a general way it is benign. Until comparatively recently I considered pemphigus of the eye as an entity, but not the pemphigus as it appears on the skin.

Pityriasis-Rosea-Like Eruption from Gold Salts; Lichen-Planus-Like Eruption from Gold Salts.

G. E. M., a 55 year old white man, reported on Aug. 11, 1942 because of lesions in the mouth. There is a history of arthritis for the past eighteen months, for which his home physician gave him eight weekly injections of gold salts in April and May of 1942. The injections were discontinued because of the appearance of the lesions in the mouth. Two weeks later red, scaling, severely itching papular lesions appeared on the hands and feet and gradually spread over the entire body. At first the appearance of the eruption resembled that of pityriasis rosea, but recently papules suggestive of lichen planus have developed. Not all of the lesions are lichenoid, and the macular pigmentation has been fading during the past week.

DISCUSSION

DR. CLARK W. FINNERUD, Chicago: The disease in this case is one of the largest of my numerous question marks. I am sure any one could take the present eruption for lichen planus, but it would be unusual to see true lichen planus of this extent without any evidence of involvement of the mucous membranes. The section corresponds with the diagnosis of lichen planus. In view of the history, gold salts certainly should be strongly suspected as being the cause, but my impression is that this might be an eruption—whatever it is, possibly lichen planus—occurring irrespective of the injection of gold salts.

DR. HENRY MICHELSON, Minneapolis: I think all the members have seen lichen-planus-like eruptions evoked by drugs. I think that arsenic is the most common one to cause this, but occasionally it may be due to bismuth. I have not had the same experience that Dr. Finnerud has had as regards involvement of the mucous membranes. I have encountered many cases of widespread lichen planus without lesions on the mucous membrane, and I should not use their absence as a diagnostic point.

DR. PAUL A. O'LEARY, Rochester: I think the enthusiasm with which gold salts are being used by internists in treating arthritis is going to produce many cases of dermatitis. The use of gold salts in initial doses of 100 mg. and larger or like amounts two or three times a week, I fear, will lead to complications of this type as well as certain of the blood dyscrasias. In my experience gold salts are too potent to use indiscriminately and in such large doses without proper preparation of the patient.

DR. HARRY R. FOERSTER, Milwaukee: The features of pityriasis rosea and the extensive involvement of the face are opposed to a diagnosis of lichen planus.

I believe this patient has a medicamentous eruption with lichen-planus-like lesions, as seen following arsenical medication.

Dr. Francis W. Lynch, St. Paul: I think there are additional points against this condition's being a true lichen planus. With an eruption of this extent one would expect more grouping over the flexor surfaces and the sacrum; here the eruption is diffuse. The changes in the nails are not characteristic of lichen planus, although there are some linear striations and minute pits. Many of the pits are linear instead of being like pinpoints; many are not continuous from the base to the end of the nail but occur in short segments, which might represent the effect from repeated insults, such as might occur after a series of injections.

Dr. Carl W. Laymon, Minneapolis: Cases like this make one wonder whether this disease is true lichen planus occurring coincidentally with the administration of gold salts or dermatitis medicamentosa simulating lichen planus. I think that one may say that there are eruptions produced by gold salts or arsenicals which are completely indistinguishable, both clinically and histologically, from true lichen planus.

Dr. Louis A. Brunsting, Rochester: Originally there was considerable pruritus and the lesions resembled a papular neurodermatitis with the distribution of pityriasis rosea. The progress was slow with gradual improvement, and the resemblance to lichen planus has become apparent only in the last ten days.

Disseminated Neurodermatitis with Early Cataract.

J. C., an 18 year old white man, came here on Aug. 19, 1942 because of generalized lichenified dermatitis, which has been widespread for the past two years. There is a history of mild asthma between the ages of 8 and 14 years and infantile eczema between the ages of 2 and 3 years. The latter condition did not recur until the patient was 10 years old, when the flexural aspects of both arms became involved. After a six year period of freedom, there was another recurrence following a summer of exceptional activity and mental tension. Intradermal and scratch tests made two years ago showed positive reactions to pork and some citrous fruits; however, this is not borne out by the patient's experience. There is a history of hay fever in the family.

On examination the patient presented a generalized erythematous eczematoid dermatitis with universal pigmentation and considerable lichenification on the flexural surfaces of the extremities and on the neck. There were some superficial scaling on the trunk and weeping around the neck and forearms. Examination of the eyes revealed incipient cataract of the right lens.

After seven weeks in the hospital and treatment with soothing agents, autohemotherapy and histamine diphosphate intravenously, the erythema, pruritus and lichenification have diminished.

DISCUSSION

Dr. Ruben Nomland, Iowa City: I have recently encountered a case in which this disease occurred in twins, who are now in their thirties, both of whom had the entire syndrome, which Dr. Brunsting should discuss because he has written about it.

Dr. S. E. Sweitzer, Minneapolis: I should like to register an objection to the term disseminated neurodermatitis. Every one knows that this disease starts as a food allergy in infancy; the patients usually have remissions and relapses and acquire a sensitivity to various substances with which they have contact as they go along. Finally, most of them get well before the age of 30. No evidence has been offered that proves a neurogenic origin for this disease. The name atopic dermatitis is a good designation.

Dr. Paul A. O'Leary, Rochester: Are cataracts in association with atopic dermatitis or neurodermatitis really common, or are they common only at the clinic?

DR. RUBEN NOMLAND, Iowa City: Dr. O'Brien, head of the department of ophthalmology in Iowa City, who has had a large experience, was unfamiliar with the syndrome. He had a patient with it for the first time two or three months ago.

DR. OLIVER S. ORMSBY, Chicago: The point I want to bring up is relative to cataract's being produced by roentgen rays, and I should like Dr. Brunsting to discuss this point further. I have seen several patients with atopic dermatitis in whom cataracts developed later. I am sure some oculists are imbued with the idea that cataracts develop in patients with this disease as the result of treatment with roentgen rays. I think there is no connection in the major portion of these cases.

DR. LOUIS A. BRUNSTING, Rochester: Of the more than 40 cases of cataract I have observed in connection with this syndrome, in some it was advanced to a state of complete blindness while in others the opacity was detectable only on slit lamp examination. All patients with this condition are given a slit lamp examination. Apparently, there is no correlation between the degree of cataract and the extent of the dermatitis, for a typical cortical opacity may be found in the lens when there is only mild lichenification of the flexures of the arms and legs. Eight patients of this group in whom cataracts developed had never been exposed to roentgen treatment to the face, and similar instances have been reported by others; nevertheless, it is well to avoid the use of such treatment when the vision is involved in order to avoid medicolegal complications. No one knows why such cataracts develop: whether they are due to a deficiency, a congenital predisposition or a protein reaction of sensitization in which both the lens and the skin are involved.

Ragweed Dermatitis.

E. K., a 52 year old farmer, presents chronic, crusted and lichenoid dermatitis distributed over the face, neck and extremities and sharply delimited to these sites. The present condition began in the late summer a year ago during the haying season and has persisted. For three or four years preceding the onset there had been dermatitis in the same sites occurring each August but lasting only a few weeks. There is no history of allergic disturbance, such as asthma or hay fever, in the patient or the family. The general physical condition is good. Patch tests with common weeds showed a positive reaction to the following ones: pyrethrum 1 plus, small ragweed 2 plus, burweed marsh elder 1 plus and cocklebur 2 plus. The reactions to other patch tests were negative.

DISCUSSION

DR. RUBEN NOMLAND, Iowa City: Ragweed dermatitis is fundamentally a dermatitis of farmers. It is easy to recognize clinically, and a great deal of it is seen. The diagnosis can be proved, as in this case, by a patch test of ragweed extract, which can be made very easily according to the technic described by Dr. Bedford Shelmire. I have treated a number of patients with ragweed dermatitis by giving ragweed extract in oil in fairly large doses—up to 40 or 50 drops of a 1 to 100 solution of ragweed extract in oil—and one can obviate the symptoms of ragweed dermatitis in a great many patients. As a matter of fact, about three fourths of them have only a few symptoms during the worst season, which is in August; so it is worth while to give them a trial of the oil extract. One must be careful not to give it when the condition is too active. It is best to give it before the season starts, if possible; however, it can be given early in the season when the trouble is mild. The patients will have to take the oil extract indefinitely during the active season. I have followed some of these patients for four years, and every year it is necessary for them to take the extract to control the dermatitis.

DR. S. E. SWEITZER, Minneapolis: Ragweed dermatitis in a farmer is not a simple problem. Usually there is a history of dermatitis starting in August

and getting better in the fall and winter. The next year it gets worse and the attack lasts longer as the farmer gets a little pollen from the hay and other contacts in the barn. I do not think that such a patient can be desensitized; he has to change his occupation and keep away from pollens or he gradually gets a generalized dermatitis and has to stop work.

DR. STEPHAN EPSTEIN, Marshfield, Wis.: Ragweed dermatitis is especially interesting. When I first observed cases of it I always thought it was atopic dermatitis. The location is that of atopic dermatitis, and when the acute features subside it resembles this condition even more; yet in most of the cases it is a contact type of dermatitis. There are two types of ragweed dermatitis: one a contact type, which gives a positive reaction to patch tests with the oleoresins, and the other an atopic type, which gives a positive reaction to scratch or intradermal tests with the ragweed proteins. Worst of all is a combination of these two types.

Cases of this condition are also interesting from a theoretic point of view. They demonstrate instances of atopic dermatitis in adult life when the allergic mechanism is the chief factor. On the other hand, they indicate that other factors play a role also. Dr. Nomland and Dr. Sweitzer mentioned cases in which there are symptoms the year around. Sometimes one may test for oats and hay and get a positive reaction, only to find later that it was the ragweed in the oats and in the hay which caused the reactions. But there are other instances which are difficult to explain. Dr. Brunsting and Dr. Reuter will remember a case which was taken before the Industrial Commission. A patient had a typical ragweed dermatitis; yet outside of the season he had recurrences without contact with ragweed. No one was able to find the reason for his trouble. Whether a case of this kind represents an instance of multiple sensitivity which cannot be demonstrated or whether nonallergic factors contribute to the recurrences, I do not know.

DR. HARRY R. FOERSTER, Milwaukee: Disseminated neurodermatitis and ragweed dermatitis may be properly discussed together because of similarities in behavior, even though the mode of allergenic sensitization differs at the onset, the former being due to ingestion or inhalation and the latter to contact. In both, multiple sensitivities develop through years of repeated exposures to the original agent and to miscellaneous secondary allergenic agents. Ragweed dermatitis often persists through the winter because of secondary contact sensitization to which the farmer is exposed, and the patient with neurodermatitis may also acquire contact sensitivities. In this respect such a patient resembles the industrial worker in whom multiple sensitivities develop not all due to industrial exposure. These multiple sensitivitities confuse the interpretation of cutaneous tests and raise a question as to the effectiveness of desensitization treatments. I believe disseminated neurodermatitis to be a better designation than atopic dermatitis for the former of these two conditions, because neurogenic factors play an important part in the rubbing and scratching that produce or intensify the dermatitis.

DR. LOUIS A. BRUNSTING, Rochester: It is important to test patients with this condition with a variety of weeds of the ragweed group, such as small ragweed, western ragweed, southern ragweed, burweed marsh elder and cocklebur, and also with the sages and pyrethrum. Giant ragweed rarely elicits a reaction in the patch test. The pollen or the leaf may be used for testing as well as the diluted oil. I have not been satisfied that the use of oil by mouth reduces the degree of sensitivity, for the reaction to the patch test remains much the same after treatment as before and there is a good deal of spontaneous variation in the recurrences, depending on the season, the location of the patient and the skill he acquires in caring for his skin once he recognizes the offending agent.

Exfoliative Psoriasis.

Mrs. G. S., a white woman aged 72, was admitted to the hospital on Sept. 17, 1942 with a universal exfoliative erythroderma and moderate pruritus. The onset began in 1939, with an erythematous weeping dermatitis of the forehead, neck and ears, which was suspected of being precipitated by a recently dyed hat. After several exacerbations and remissions, the groin also became involved, and gradually a generalization followed reactions to application of 30 per cent sulfur ointment and administration of iodides by mouth. The patient recalls that she always has had a "sensitive skin." There was no personal or familial allergy except for one episode of urticaria in 1939.

The results of physical examination were essentially normal except for a moderate lymphadenopathy. The results of examination of the blood were normal except for a mild eosinophilia.

Therapy has consisted of application of 1 per cent crude coal tar ointment and ultraviolet irradiation, with steady improvement in the condition of the skin.

DISCUSSION

DR. MAURICE J. REUTER, Milwaukee: Because of the history, I feel that the patient probably had a sensitization dermatitis. Her condition began as an inflammatory, weeping eruption about the face, and subsequently a generalized dermatitis developed. I should like to suggest this as a diagnosis rather than exfoliative psoriasis, although the biopsy report is in favor of psoriasis. I think that perhaps too much stress is being laid on biopsies.

DR. PAUL A. O'LEARY, Rochester: I realize there is a question in the minds of some as to the justification for the diagnosis of psoriasis. When I first saw the patient, the diagnosis of psoriasis was suggested by the generalized erythroderma characterized by a heavy mica-like scale, little pruritus and little complaint as to her skin, although she is 72 years old and had been traveling for three days on a train, so that her skin had received little attention. In fact, she was quite pert in spite of the universal eruption. The histologic section favors the diagnosis of psoriasis, and her response to the Goeckerman regimen has been what one might expect in this disease.

Dermatomyositis.

Mrs. C. B., a 36 year old white woman, was first seen here on Oct. 5, 1942. In November 1942 there appeared mottled redness of the hands and fingers with soreness and discharge around the nail beds; this has continued. In December 1941 there were aching and soreness in the muscles of the legs, thighs, shoulders and, more recently, arms. In April 1941 there was swelling of the face and hands with pigmentation of the face and neck. From time to time during the past year and a half there have been ulcerative areas on the knuckles, ears and face leaving scars. In the past few months there have been generalized weakness and muscular soreness with some dysphagia. There also has been a slight febrile sensation on frequent occasions, usually in the evening. In 1938 the patient had an abscess of the cheek following dental extraction. In 1939 there was spontaneous abortion at six weeks and in 1940 a miscarriage at eight months due to premature suppuration of the placenta. The family history is irrelevant.

She has a temperature of 99.5 F. There is edema of the face and hands with mottled edema of the hands and fingers. The eyelids have a heliotrope hue, and there is a bronze pigmentation of the face, neck and exposed V of the chest. There are many atrophic, shiny, deeply pigmented plaquelike areas 1 by 1 cm. with telangiectatic borders on the knuckles, face, neck, chest and left eyelid. Deep tenderness is present over the biceps, anterior tibial, thigh and shoulder muscles. Routine studies showed that the urine and blood were normal, and the Kline, Kahn, Hinton and Kolmer reactions were negative. The blood urea was 22 mg.

per hundred cubic centimeters, and the sedimentation rate was 14 mm. per hour. The results of special studies of the urine and the differential blood count were as follows:

Urine volume	1,740 cc.
Creatine in 100 cc.	12 mg.
Creatine in specimen	217 mg.
Creatinine in 100 cc.	50 mg.
Creatinine in specimen	877 mg.

Leukocytes	8,100
Lymphocytes	13 per cent
Monocytes	4 per cent
Neutrophils	80 per cent
Eosinophils	3 per cent

Dermatomyositis.

M. B., a white girl aged 9 years, first had general fatigue and a sense of weakness of the legs fourteen months prior to admission. The daily temperature was slightly elevated and ranged between 100 and 101 F. About this time the first signs of pain and stiffness and immobilization of the joints of the upper and lower extremities developed, but she has had no pains in the joints for the past five or six months.

Physical examination revealed a well developed, poorly nourished child with limitation of motion of all the joints. The skin is dry and hot; there is a mottled reddish brown pigmentation with disseminated areas of depigmentation and telangiectasia of the face, upper part of the chest and parts of the lower part of the trunk. There is pronounced stony hard induration of the musculature, which is nodular at some tendinous attachments, associated with relative general muscular atrophy. A roentgenogram of the extremities showed areas of subcutaneous calcification.

Dermatomyositis.

A. E., a 15 year old school girl, first presented herself on June 12, 1936, with a history of having been ill for two months with pain and swelling of multiple joints and a fever, with a temperature of 100 to 101 F. When she was examined here she did not appear acutely ill. There were erythematous plaques distributed over the entire body surface, including the face, with painful elbows and ankles. Examination of the heart showed gallop rhythm with a soft systolic murmur at the apex. The urine was essentially normal, and the red blood cells numbered 3,410,000 and the white cells 5,900, with 14.5 per cent eosinophils. A blood culture made on July 27, 1936 gave negative results.

On Jan. 7, 1936 the biceps and hamstring muscles were tender and there were definite muscular weakness and atrophy. About this time edema of the face developed with extension of the plaques on the trunk and extremities with gradual coalescing. On Aug. 9, 1939 there were increasing weakness and atrophy with limitation of motion due to muscle contracture. When examined here on July 20, 1942 she showed hirsutism, a hypertrophied clitoris and a scrotum-like appearance of the labia. She had menstruated only once, in November 1941.

At present there is decided muscular atrophy and some muscles are thin fibrous bands. The arms and legs are now ankylosed in complete flexion. This patient was presented before this society on Sept. 24, 1939 and is presented again today to show the severe deformities that this disease may produce.

A specimen for biopsy taken on June 13 from one of the erythematous plaques showed a microscopic picture of toxic dermatitis. There was no definite evidence of lupus erythematosus.

DISCUSSION OF THREE CASES OF DERMATOMYOSITIS

DR. MORRIS WAISMAN, Chicago: The last of the 3 cases of dermatomyositis is of special interest because early the eruption suggested acute disseminated lupus erythematosus. On the basis of similar cases, a considerable literature has arisen concerning a presumed relationship between lupus erythematosus and dermatomyositis, eruptions of this kind being regarded as "transition" forms between the two diseases; but it can be demonstrated that while clinically the eruption in dermatomyositis may resemble that of lupus erythematosus the histologic characteristics of lupus erythematosus are absent and the actual cutaneous diagnosis is simply that of toxic dermatitis. On the other hand, as Dr. Montgomery has shown, in cases of acute disseminated lupus erythematosus the skeletal muscles show no significant alteration microscopically. Therefore, by histopathologic study of skin and muscle one can readily differentiate conditions which clinically have much in common. Incidentally, it is important to observe that the features of lupus erythematosus in this girl have now entirely disappeared.

DR. PAUL A. O'LEARY, Rochester: We presented these 3 patients to show some of the phases of dermatomyositis and to call attention to the fact that although the disease may cause death it also may produce a severe and totally incapacitating type of invalidism. I had hoped also to present a child who has a severe calcification of the skin, a universal process with total disability of a different nature than any of these present. However, she was unable to be present today. Our knowledge of the cause and treatment of this disease is still lacking, and we are encountering more cases each year.

Acrosclerosis (Sellei).

S. B., a 44 year old woman, a minister's wife, came to the clinic on Oct. 9, 1942 because of flushing of the face and hands and swelling of the face, chin, forearms and fingers, with a drawn feeling in these areas. There is a history of onset in the fall of 1941 with involvement of the fingers and hands. Cold weather produced changes in color and pain in the fingers; swelling, stiffness and tenderness appeared subsequently. During the five months preceding admission the face and neck became similarly involved with swelling, and a taut feeling was noted, especially in the morning on arising. There were flushing and pigmentation of the face, neck and upper part of the chest and some dysphagia. There is a history of psoriasis since the age of 15, but there have been no cutaneous lesions during the last year. Recently psoriatic changes have been noted in the finger and toe nails.

Examination shows binding of the skin over the hands, fingers and lower parts of the forearms, with similar sclerodermatous changes over the face, neck, upper part of the chest and shoulders. There are a diffuse brownish pigmentation of the face, neck and upper part of the chest and stiffness, tenderness and swelling of the hands and fingers. Psoriatic changes in the form of yellowish discoloration and pitting are present in the finger nails and toe nails.

Localized Scleroderma (Morphea).

Mrs. L. N. T., a white woman aged 31, was seen here on Sept. 7, 1942, at which time she stated she was suffering from arthritis. At the age of 14 she noted the appearance of a white, slightly infiltrated area of skin on the chest; at the age of 29 she first noted stiffness and limitation of motion of the fingers and toes. Questioning revealed that there was little pain on flexing the joints but merely tightness of the overlying skin. The hands were painful when cold. During the six months preceding admission several white, glistening, firm patches of skin appeared on the chest; these subsequently became pigmented.

The results of flocculation tests and a roentgenogram of the chest were normal. The basal metabolic rate was + 4 per cent. Dark adaptation tests revealed defi-

nitely reduced function; the patient required three to four times as much light as the ordinary person to see in the dark. Roentgenograms of the left foot and lumbar portion of the spine were normal.

Acrosclerosis (Sellei).

M. C., a white woman aged 39, has been seen here on numerous occasions since her first admission, in December 1939. There is a history of gradual onset three months prior to admission of stiffening of the skin of the face, forehead, breasts and fingers associated with pain and whitening of the fingers, which when warmed became painful, cyanotic and red. There had been chilblains of the feet for many years. At the time of our first examination her temperature was 99.7 F. and pulse rate 100. There were a woody hardness with binding down of the skin symmetrically over the entire face, upper half of the chest and breasts and acrocyanosis and coldness of the extremities. There was a thyroid adenoma, grade 1 plus, and reactions to Allen tests were negative. The results of laboratory examinations were entirely normal except for slight tapering of the terminal phalanges of the fingers, as shown by roentgen examination. Treatment was advised by means of local application of heat, massage and administration of pituitary extract five times a week for approximately a hundred injections.

For the next two years the patient returned at six month intervals for observation, and each time we noted evidence of decided improvement. Specimen taken for biopsy in December 1939 from the lesions on the chest and the left hand revealed atypical acrosclerosis.

DISCUSSION OF CASES OF ACROSCLEROSIS (SELLEI) AND CASE OF MORPHEA

DR. MORRIS WAISMAN, Chicago: It may be pointed out that although morphologically the cutaneous changes are those of scleroderma, there are several reasons for segregating this type (acrosclerosis) and giving it a special name. To begin with, I think patients have a distinctive cause for acrosclerosis, a vasomotor abnormality, as shown by preliminary symptoms of the Raynaud type. There are probably various causes for scleroderma, which may in general be classified under the broad headings of vascular or vasomotor and metabolic; acrosclerosis includes only conditions of vasomotor origin. Secondly, the typical onset of symptoms and the course and distribution of the sclerosis distinguish this type from other forms of scleroderma. And, finally, the tendency to spontaneous arrest and the good prognosis with regard to life stamp acrosclerosis as an essentially benign disease.

DR. PAUL A. O'LEARY, Rochester: The 3 patients with acroscolerosis were presented in an effort to show the difference between this disease and generalized scleroderma. One has early acrosclerosis; the second patient presents the arrested form of the disease, and the third has had morphea for seventeen years while the acrosclerosis is of two years' duration.

The first patient, who shows the early phase, has had stiffening of the hands for about ten months. She had noticed swelling of the face but was unaware of the contracture of her lips until we called her attention to it. The diagnosis of an "arthritic" condition had been made at home because of the pain in the finger joints and the inability to make a fist.

The woman with the morphea has had it for seventeen years. Less than two years ago she began to have what was thought to be arthritis, because of pain and swelling of the hands. At this time she noted also for the first time evidence of Raynaud's disease. She had a decided reduction in dark adaptation, which has cleared up with the administration of vitamin A and is not related to the cutaneous disease. Prostigmine and massage to the hands made them 60 to 70 per cent better, so that today one may be somewhat justified in questioning the diagnosis of acrosclerosis.

The third patient presents an arrested form of acrosclerosis. She is a comptometer operator and was unable to work for one and a half years but has now

returned to the same position after a course of treatment consisting of administration of prostigmine, heat and massage, which seems to offer the best therapeutic program for this disease. Prostigmine methylsulfate is given in a 1 to 2,000 dilution, 1 cc. a day, prostigmine bromide by mouth, 15 mg. three times a day, and papaverine hydrochloride, 0.25 mg. three times a day, and daily heat and massage. This therapeutic program is not a panacea for this disease, and in certain patients the condition is arrested spontaneously. I believe that is one of the things which must be emphasized about acrosclerosis and which helps to distinguish it from generalized scleroderma. I realize that many physicians do not distinguish this syndrome from scleroderma; however, the distribution of involvement to the face, the upper part of the chest and the forearms, the absence of boardlike sclerodermatous infiltration, the course of the disease, which if mild may arrest itself spontaneously or if severe results in gangrene and spontaneous amputation of the fingers, are not common to generalized scleroderma. The vasospastic phenomena occur rarely in generalized scleroderma, and only 15 per cent of the patients with Raynaud phenomena show these cutaneous changes. Sclerodermatous infiltration of the esophagus, as illustrated by the first patient, is not uncommon in acrosclerosis, and the disease is seldom encountered in men. The use of prostigmine has in my experience been of no value in scleroderma, while it is of help in acrosclerosis. These are some of the reasons that I distinguish this disease from ordinary or generalized scleroderma.

Acrodynia.

E. H. P., a child aged 3 years, of normal birth (weight 7½ pounds [3,400 Gm.]) and bottle fed, has a history of much vomiting as an infant. The baby walked and talked at 11 months; colds were infrequent, and there were no sore throats.

About eight weeks ago the baby was taken to a physician because of smegma under the prepuce. There was loss of appetite, the child was irritable and spent most of the day in bed. He would take only a little milk. There is a history of photophobia, excessive perspiration, cold hands and feet, some redness of the palms and soles and recently peeling of the hands and feet and erythema of the digits. Anorexia was noted, and at one time the child had a rash on the trunk.

Examination shows the aforementioned features, including slight changes in the gums. The blood pressure was elevated, but there were no other findings of significance. The results of neurologic examination were essentially normal. Treatment has consisted of administration of vitamin B complex and a high caloric diet.

DISCUSSION

DR. HENRY MICHELSON: I have had the privilege of observing a number of cases of acrodynia and had the occasion to look up the disease carefully. In this patient I did not see any of the classic signs of acrodynia, but he may have been cured. I have no fixed idea about the cause. At the time when the disease was attracting a great deal of attention, focal infection was looked on as the cause. The history of the disease, its occurrence in prisons and military camps in France and the later observations might point to a vitamin deficiency.

DR. HAMILTON MONTGOMERY, Rochester: When I first saw this patient on admittance two weeks ago, he had cold, clammy hands, was restless and irritable, hid his head and had evidence of photophobia. Dr. Kennedy, who has observed many cases of acrodynia in the pediatric service had no question about the diagnosis at that time, nor did I. There has been decided improvement following the administration of vitamin B complex.

DR. LOUIS A. BRUNSTING, Rochester: What is the relationship between acrodynia and beriberi?

DR. HAMILTON MONTGOMERY, Rochester: The disease in this case started rather late compared with most cases of acrodynia, in which onset occurs in early infancy. Perhaps this accounts for the more rapid response to treatment.

DR. OLIVER S. ORMSBY, Chicago: The physicians who are doing the most work on acrodynia are divided in their opinions as to the role that vitamins play. Some believe that the disease interferes with the absorption of vitamins, while others believe that it is an avitaminosis.

DR. FRANCIS W. LYNCH, St. Paul: Changes which pediatricians frequently regard as early evidence of acrodynia are also observed in children who present a condition which I think represents neurodermatitis. I wonder if the improvement might not be related to hospitalization and getting away from the family. It seems to me that children like this usually have mothers who are tense, upset and extremely anxious about their children. I cannot be sure that this child has had acrodynia.

DR. HARRY R. FOERSTER, Milwaukee: I reported a series of cases of acrodynia some years ago (ARCH. DERMAT. & SYPH. **12**:17 [July] 1925) and recall the controversy over causation and therapy. At that time avitaminosis was suggested by some observers as the probable cause, and the only readily available vitamin therapy was cod liver oil and viosterol. If this case were a typical one, the rapid improvement should be credited to vitamin B complex therapy. I think acrodynia is an entity, and I believe it is a deficiency disease and that it should therefore not be grouped with the neurogenic dermatoses.

Chronic Disseminated Lupus Erythematosus.

Mrs. J. D., a white woman aged 48, reported in August 1939 because of erythematous areas about the forehead, face and neck of two and a half months' duration. There is a past history of radical mastectomy for carcinoma in 1936.

Examination at that time showed a ring of erythema on the forehead at the hair line and similar streaks on the face, near the nose, on the V area of the neck and on the cervical region. In April 1940 there appeared a reddish, purplish, mottled lichen eruption on the face, arms and knuckles, with marked asthenia. At that time biopsy was performed.

The general health was built up without difficulty. Treatment was given by injections of gold salts intravenously in 1940 and two courses of quinine in 1940. Since then there has been occasional flushing erythema of the face and neck with monthly edema of the face and neck, nasal congestion and slight epistaxis and recently some telangiectasia and added sclerodermatous lesions.

In September 1940 there was complicating phlebitis of the arm, and the patient had toxic erythema of three days' duration in October 1940, while taking the second course of quinine.

The results of laboratory studies were essentially normal throughout. The white blood cells ranged between 11,200 and 4,400, the latter count on Sept. 24, 1940.

DISCUSSION

DR. CLARK W. FINNERUD, Chicago: I am particularly interested in the section in that it carries out beautifully the description of Montgomery and Goeckerman a few years back.

DR. RUBEN NOMLAND, Iowa City: I had a patient who was in the hospital here for six months about fifteen years ago with a diagnosis of disseminated lupus erythematous, and she was given an extremely unfavorable prognosis. She is now 76. She still has red, slightly scaly lesions and atrophic areas, as does the patient presented. A biopsy was performed recently; the slides were shown to Dr. Montgomery, and I believe he still thinks the microscopic picture is that of disseminated lupus erythematosus. Apparently, there must be a benign type of disseminated lupus erythematosus that runs a chronic course and has a moderate amount of atrophy, redness and scaling but no systemic reaction. She does not have a leukopenia or any of the other symptoms associated with disseminated lupus erythematosus.

DR. HAMILTON MONTGOMERY, Rochester: One can distinguish histologically between the chronic discoid and the disseminated form of lupus erythematosus,

but in the majority of the series of cases I have studied I have not been able to predicate on histologic grounds alone a distinction between the various types of disseminated lupus erythematosus.

Acne Varioliformis.

J. E. J., a 49 year old white man, was first seen here on Oct. 5, 1942. He presented papular, pustular and pitted scars on the face, neck and scalp of two to three years' duration, most of the pitted scars being pronounced along the hair line.

Lichen Nitidus; Acne Varioliformis.

J. R., a man aged 29, a physician, is presented because of an eruption of six months' duration, consisting of tiny lichenoid papules distributed chiefly over the flexor surfaces of the arms, forearms and lower parts of the legs. Biopsy was made of a lesion on the left knee. Scattered over the scalp, face, neck and upper part of the trunk are scars of healed acne varioliformis of some twelve years' duration. This disease was benefited considerably about a year ago by the nonspecific administration of neoarsphenamine.

DISCUSSION OF CASES OF ACNE VARIOLIFORMIS

DR. HENRY MICHELSON, Minneapolis: What do you think of the use of sulfonamide drugs in the treatment of this condition?

DR. LOUIS A. BRUNSTING, Rochester: We have used sulfonamide compounds internally in the treatment of acne varioliformis without any appreciable benefit.

DR. JOHN F. MADDEN, St. Paul: Recently I have used 5 per cent sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) ointment locally, and in most cases it undoubtedly causes the acne varioliformis to heal and will keep it healed if an occasional application is used. The use of neoarsphenamine may produce temporary but not permanent benefit. All patients that I have followed over a long period have had recurrences at varying intervals. Neoarsphenamine certainly is a dangerous drug to use on a comparatively harmless eruption.

DR. STEPHAN EPSTEIN, Marshfield: I have been using 5 per cent sulfathiazole ointment recently; now I am combining 5 per cent sulfur and 5 per cent sulfathiazole. Sulfathiazole can be applied well also in a 2 per cent alcoholic solution. The result has not been superior to treatment with sulfur, which is the preparation of choice for treatment of this condition. I should like to ask Dr. Montgomery about his opinion as regards the relation of acne varioliformis to acne necrotica miliaris. Treatment of acne varioliformis is nearly always successful when continued for several weeks after the clinical symptoms have disappeared; but in my experience the same method rarely produces a permanent cure in the miliaris type.

DR. HAMILTON MONTGOMERY, Rochester: In the treatment of acne necrotica miliaris ointments containing sulfur or strong ammoniated mercury ointment, in my experience, have worked satisfactorily. This disease and acne varioliformis are closely related, both being essentially follicular pyodermas but differing in the size of the lesions and their distribution.

Necrobiosis Lipoidica Diabeticorum.

V. R. S., a white man aged 31, reported here Sept. 25, 1942. According to the history, he first noticed a dime-sized red area aver the medial aspect of the right ankle in February 1942. A month later four similar but smaller lesions appeared on the lateral aspect of the lower part of the right leg. All were asymptomatic and have remained stationary as regards size and color. There is a history of diabetes of six years' duration, for which the patient received 45 units of protamine zinc insulin.

Examination shows the patient to be well developed and well nourished. He presents several discrete brownish yellow plaques on the right leg. There are three lesions on the lateral and one on the medial aspect of the extremity, varying from 1 by 1 cm. to 2 by 3 cm. in diameter. The fasting blood sugar is 109 mg. per hundred cubic centimeters.

DISCUSSION

DR. HAMILTON MONTGOMERY: This patient presented some lesions that were suggestive of granuloma annulare. Ellis (ARCH. DERMAT. & SYPH. **43**:822-829 [May] 1941) suggested that granuloma annulare and necrobiosis are the same disease. Prunty and I (ibid. **46**:394-414 [Sept.] 1942) found that mucicarmine stains were positive for mucin in histologic sections of granuloma annulare and that mucin could not be demonstrated in cases of necrobiosis. The histologic picture of the eruption otherwise is similar, but in granuloma annulare one rarely finds extracellular deposition of lipids. At the time the biopsy was performed this patient had a normal blood sugar content. The histologic picture showed typical changes of necrobiosis with extracellular deposits of lipids. The mucicarmine stains were negative for mucin. I think these two diseases are entirely distinct from one another.

Mycosis Fungoides.

C. D. F., a man aged 53, a farmer, was first seen here in June 1937, when a diagnosis of mycosis fungoides was made. In 1906, when he was 17 years of age, an elevated, circumscribed, brown, smooth spot developed on the anterior surface of the left thigh, which persisted. In 1916 elevated scaly plaques appeared on the body. The lesions were worse in the fall of the year and improved some in the summer. There was slight pruritus. There was no history of medication prior to admission.

Examination showed reddish brown macular spots on the trunk, forearms and feet with some lichenification and scaling of the larger lesions. The results of general examination were normal. The urine, the blood and a roentgenogram of the chest were normal. Three different biopsies showed varying features of mycosis fungoides.

From 1937 to 1941 the patient was treated with roentgen rays with good results, receiving on the average of two to three treatments each year. The lesions thinned out considerably, there was less pruritus and in 1938 only a few plaques were present on the back. The blood counts, differential ratio and roentgenograms of the chest remained normal during the course of treatment. In December 1941 eight artificial fever treatments were given because of inability to control the pruritus and the appearance of new lesions with roentgen rays.

The condition is now in partial remission and he is comfortable, although the clinical features of mycosis fungoides are obvious. He has not been given ethyl chaulmoograte.

Mycosis Fungoides.

C. F., a 43 year old man, first came to the clinic in August 1942. In May 1941 some irregularly shaped erythematous plaques developed on the back; there was no associated pruritus. A diagnosis of mycosis fungoides was made by Dr. Foerster in December. Since that time the patient has had roentgen therapy in conjunction with the administration of acetarsone.

After admission here, he was given a series of eight hyperthermy treatments and a series of fifteen injections of ethyl chaulmoograte. He has continued taking ethyl chaulmoograte and is presented today to demonstrate the effect of fever therapy and this drug in the treatment of mycosis fungoides.

DISCUSSION OF CASES OF MYCOSIS FUNGOIDES

DR. HARRY R. FOERSTER, Milwaukee: I am interested in these patients because of having referred one of them to Dr. O'Leary. I had treated him with roentgen rays and pills containing arsenic (asiatic pills), and he went through the usual

course, showing gratifying response to initial roentgen therapy and then reverting to a phase in which the lesions become resistant. At the time of coming to the clinic he was taking acetarsone and showing benefit from it. I am impressed by the improvement in his condition following fever therapy and injections of ethyl chaulmoograte.

DR. PAUL A. O'LEARY, Rochester: The use of a chaulmoogra oil derivative in the treatment of mycosis fungoides was suggested by Lumholt of Denmark. We use fever therapy in combination with ethyl chaulmoograte. The treatment consists of approximately eight hyperthermy treatments at the rate of two or three per week. During the fever course, or shortly thereafter, the administration of ethyl chaulmoograte is started, increasing doses being given until the patient is receiving 5 cc. intramuscularly every day. Approximately twenty injections constitute a course, and some patients have been given four courses of the drug. I have no concept of the *modus operandi* of this program, but I am now convinced after having treated and observed some of these patients for seven years that it offers the patient with mycosis fungoides some relief. It is not a panacea for the disease, and in a few patients in the advanced phase of the disease it did not arrest the progress. However, for those in the early stages it is another method of treatment to augment roentgen therapy.

There is no question in my mind that for patients with mycosis fungoides who have become unresponsive to roentgen rays and who are suffering from severe pruritus this combined treatment gives relief from the itching and makes them responsive to roentgen therapy when applied to the individual plaques. In some patients a spontaneous involution of the lesions has occurred, lasting sometimes as long as six months. The first of these 2 patients has had the disease for about a year and a half, and it has been progressing rapidly, while the second patient has had the disease for approximately thirty-five years, in any event twenty-six years, and it is running a mild and protracted course. In the case of the former patient the effect of this combined treatment augmented by roentgen therapy will warrant long observation, while in the latter patient not much change is to be anticipated, because he presents the mild type of the disease. May I repeat for emphasis that this therapy is not a cure-all for mycosis fungoides but is a means of giving symptomatic relief when roentgen therapy fails?

DR. W. C. POPP, Rochester: I can only reiterate what Dr. O'Leary has said about superficial therapy for mycosis fungoides. Several years ago he and I reviewed the data on about 30 patients treated here with roentgen rays. Some had been given superficial therapy to the entire body, while others had been given superficial treatment to the isolated areas of involvement and a third group had been treated with filtered irradiation to the various gland-bearing areas, much as one would treat a lymphoblastoma. It was our feeling that superficial treatment to the various areas of involvement was quite adequate unless there was some definite adenopathy. We felt that the results in patients given treatment to the isolated areas of involvement were equal to those in patients who had generalized treatment.

Pyoderma.

E. F. W., a 32 year old white woman, unmarried, came here in April 1941, at which time she was found to have congenital syphilis. According to the history, a positive reaction of the blood was noted when she was 2 years old. Details of treatment at that time are unknown, but she has had considerable intravenous and intramuscular therapy. The serologic reactions of the blood are negative now. In 1932, when she was 22, pea-sized growths developed around the anus, and in a few weeks numerous lesions began to appear there. These became red and raw, and pus discharged from some of them; there was no pain. In 1933 the lesions were cauterized, without much improvement. From 1933 to 1941 there was slow progression of the condition. In January 1941 there were numerous blisters and a red lesion of the vulva with some ulceration and pruritus. In 1940 she was given a course of intravenous and intramuscular injections, twelve of each, in a six month period.

Examination now reveals reddish, raised, moist and ulcerated lesions, from 2 to 10 mm. in size, and many papules on the cutaneous aspect of the vulva, the folds of the buttocks and the perianal regions. Several polypoid growths are present about the anal region. Dark field examination gave negative results. There are numerous pyogenic lesions about the feet and the finger nails. Treatment has consisted of wet dressings of potassium permanganate solution and application of sulfathiazole ointment.

Acne Conglobata; Pyoderma; Hydradenitis.

L. L., a white man aged 29, first noted recurrent postauricular sebaceous cysts twelve years ago. These were followed by severe acne of the back of the neck with considerable scarring and keloidal formation. There was a gradual extension of this process to the face and upper part of the trunk, and four years ago inguinal abscesses appeared. About nine months ago transient arthritic changes of the knee joints occurred.

The physical findings on admission include the cutaneous lesions—extensive subcutaneous abscesses with keloidal scarring, intercommunicating channels, purulent to watery discharge—involving chiefly the face and neck and, to a lesser extent, the upper part of the back and chest. Multiple double comedos are present. There is limitation of motion of the knee joints; a roentgenogram indicates chiefly synovial involvement. Burrowing sinuses involve the skin of the scrotum. Laboratory tests show the concentration of hemoglobin to be 10 Gm., the basal metabolic rate—6 per cent, the reaction to a Mantoux test negative and the urinary concentration of estrogen normal. Hemolytic streptococci were cultured.

Treatment has included saucerization of the abscesses, the use of sulfathiazole, sulfur baths, roentgen therapy, ultraviolet irradiation and blood transfusions. Recently there has been a decided improvement after three weeks' use of diethylstilbestrol, 1.5 mg. daily.

Hidradenitis Suppurativa of the Axillas; Extensive Pyoderma of the Vulva.

Mrs. G. H., a white woman aged 38, was admitted to the hospital on July 29, 1942. In 1923 bilateral axillary abscesses necessitated incision and drainage; after one and a half years these finally healed, leaving considerble scar formation. In 1933 inguinal abscess and associated indolent ulcers of the thighs and legs developed (two years' convalescence). Twenty months ago an inguinal node on the left side suppurated and a burrowing abscess developed with considerable extension in spite of various forms of therapy, which included antisyphilitic therapy (although the serologic reaction was negative), roentgen therapy, use of diluted solution of sodium hypochlorite U. S. P. (Dakin's solution), irrigations, intravenous injection of gold salts, administration of staphylococcus and diphtheroid bacillus vaccines, endocrine therapy and administration of sulfonamide compounds (with reactions) and of fuadin.

Examination now reveals a massive purulent gangrenous process with intercommunicating channels involving the perineal and pubic areas and the lower part of the abdomen. Reactions to laboraory tests were negative, including the serologic tests, Ducrey and Frey intradermal tests and a fresh tissue smear for Donovan bodies. Cultures demonstrated a mixed infection with diphtheroids, micrococci, staphylococci (Staphylococcus aureus) and a gram-negative bacillus unidentified. The histologic diagnosis was reported as nonspecific granuloma.

Treatment has consisted of multiple transfusions (all with associated severe reactions), cleansing baths, irrigations with phemorol, hydrosulfosol and hydrogen peroxide. At present instillations of gramicidin (a substance isolated from soil bacilli) are being used.

DISCUSSION OF CASES OF PYODERMA AND HIDRADENITIS SUPPURATIVA

DR. JOHN F. MADDEN, St. Paul: I wonder if these patients have pyoderma, because most of the other forms of pyoderma respond to some sulfonamide com-

pound, used either externally or internally. The pyogenic organisms that are found may be secondary invaders.

DR. HENRY MICHELSON, Minneapolis: I think the second case in this group is a classic instance of acne conglobata. I believe there is a distinct relationship between all of these chronic suppurating acne-like eruptions.

DR. E. A. STRAKOSCH (by invitation), Minneapolis: I am interested in these 2 cases of extensive pyoderma because at the University Hospital topical application of sulfonamide drugs has been investigated. Topically applied sulfonamide compounds are partially inactivated by substances sometimes present in tissues, known as inhibitors. Holder and MacKay (*Mil. Surgeon* **90**:509, 1942) recently reported the combined use of urea and sulfonamide drugs in infected wounds. They knew that since urea dissolves necrotic tissue and enhances the solubility of sulfonamide compounds the added sulfonamide compounds would have a better chance to act. Dr. W. G. Clark and I investigated the action of urea in high concentration in regard to the stimulation of granulation tissue and the action on epithelization. We found that 40 per cent urea stimulates granulation tissue but impairs epithelization. At concentrations around 5 per cent epithelization is not impaired but granulation is still stimulated. In vitro studies showed that urea exerts an action which we call "anti-inhibitor." We were interested also in the action of urea on organisms resistant to sulfonamide compounds. It is likely that those organisms were made resistant because of protracted contact with sulfonamide compounds. We were able to show in vitro and in vivo that the fastness of such organisms can be overcome by the addition of small concentrations of urea (*Proc. Soc. Exper. Biol. & Med.*, to be published). We were fortunate in encountering recently 2 patients with extensive pyoderma who failed to respond to topical and oral administration of sulfonamide drugs. A strain of staphylococci recovered from 1 of these grew in a synthetic medium to which sulfonamide compounds had been added. Urea, 1.75 per cent, was capable of overcoming the resistance in vitro. Urea and a sulfonamide drug were applied locally in the aforementioned cases, and the lesions healed within a short time. A detailed report is forthcoming on these subjects in *Minnesota Medicine*. In conclusion, I should like to call attention to the fact that more and more such organisms may be encountered, and this may be the explanation for the failure of pyodermas to respond to therapy with sulfonamide compounds.

DR. RUBEN NOMLAND, Iowa City: I want to discuss the patient with the double comedos with deep-seated acne lesions. During the past year and a half I have treated a number of patients with deep-seated acne, not so severe as this, with double and single comedos. I think I have found the answer to treatment, in some of them at least, and that is to destroy the comedos. I destroy them by electrodesiccation, enough to make them inactive. In cases in which there are double comedos separated by openings about 1 mm. across—never more than 2 or 3 mm.—I desiccate the bridge. With that method of treatment I have had excellent results in mild acne conglobata. The amount of scarring produced by the desiccation is much less than that produced in the normal course of the disease.

In the case of the young man I am not sure whether that treatment would be suitable. Certainly in some of these double comedos one could break through the bridge. If the infecting organism does not fall on proper soil, namely, the comedos, it does not cause too much trouble; hence if the soil is prepared so that infection cannot take place, a great deal is done for persons with large single and double comedos. I doubt if the method is suitable for severe acne conglobata.

DR. HAMILTON MONTGOMERY, Rochester: When I saw the first patient of this group one year ago, she had definite pustules, and there was 75 per cent improvement in the lesions after five days' use of sulfathiazole ointment. However, when she returned home there was a recurrence of the lesions and she obtained no further benefit from sulfathiazole ointment. She had pustular lesions when she returned this time, and there was some response to sulfathiazole. She still has an

impetiginous lesion on the nose. The ulcers have not responded. Perhaps this patient has the resistance to sulfonamide compounds that Dr. Strakosch mentioned. Smears from the lesions were laden with streptococci. The culture reports showed a great many green-producing streptococci and a few examples of Staphylococcus aureus.

Dr. Louis A. Brunsting, Rochester: I believe more attention should be given to the soil of the host than to the type of invading organisms. This has been impressed on me particularly in dealing with cases of pyoderma gangraenosum with chronic ulcerative colitis. In cases of hidradenitis suppurativa associated with extensive acne conglobata there is an overstimulation of the apocrine and the pilosebaceous apparatus. This disease is never seen before the age of puberty, and it rarely persists after middle age. The secret of acne may be found in this group. Acne occurs most commonly among adolescents, and an acneform reaction occurs in patients who have Cushing's syndrome or tumor of the adrenal cortex or who have been subjected to therapy with testosterone. I am intrigued by the idea that this reaction may be associated with a disturbance of gonadal relationships, that is, of the balance between the secretion of androgen and of estrogen with perhaps an excess of the former. I have observed some benefit in a few cases of this type, especially that of the young man who was presented because of extensive acne and pyoderma of the face, axillas and groin, by giving diethylstilbestrol by mouth. This type of treatment should be used cautiously in carefully selected cases.

Congenital Dyskeratosis; Ectodermal Defect; Pachyonychia Congenita; Pyoderma; Corneal Leukoma.

A farmer's son, aged 19, in good general health, is presented because of disturbances of the skin which have been present more or less since birth. He is the sixth in a family of ten children, and there is no record of congenital disturbances in the family. The parents are not related. There is a history of delayed dentition. The patient has always perspired less than normal and is sensitive to heat. The hair has never been abundant. Diminished vision began in the left eye when he was 5 years old. Changes began in the nails when he was 10 years old, the nails becoming thickened and not keeping pace with the growth of the fingers and toes; there has been recurrent paronychia. When he was 9 years old vegetative lesions began on the scalp. The patient showed some evidence of mental retardation and never passed beyond the third grade in school.

Examination reveals a well developed youth with extensive pyoderma of the scalp and face. There is corneal leukoma of both eyes, with complete loss of vision of the left. The skin is yellowish, smooth and dry, and there are scattered clusters of keratotic follicular papules widespread over the trunk and extremities. There is diffuse keratosis of the hands and feet on the dorsa as well as on the palmar and plantar surfaces. The nails are dystrophic, pearly white and lifted from the nail bed in varying degrees. There is scant hair on the scalp and in the pubic and axillary areas and none on the extremities. There are bilateral nerve deafness, enlarged tonsils and diffuse fibrosis of the left lung.

Specimens for biopsy taken from the right knee, right elbow and right cheek all showed hyperkeratosis with keratotic plugging of the follicles as the essential pathologic change. Treatment during the past year has consisted of antiseptic measures to the regions of pyoderma and the administration of large doses of vitamin A by mouth and by intramuscular injection and of riboflavin by mouth, with considerable improvement in the general health but with little effect on the dyskeratosis.

Pityriasis Rubra Pilaris.

E. J. B., a 3 year old child, was first examined at the clinic on July 10, 1942, because of erythema of the palms and soles of less than one week's duration. She

was in good general health, and the results of general physical examination were essentially normal. Five days later the skin on the palms was exfoliating. There were no systemic manifestations present.

On July 18, pigmented, slightly keratotic lesions were noted on the instep, knees and elbows, behind the ears and in the gluteal cleft Bronchitis and tonsillitis developed during the last two weeks in August. During this time the cutaneous lesions improved, and on Aug. 8 the cutaneous lesions had disappeared and the skin was clear except for the changes on the palms and soles.

Large doses of vitamin A by mouth have resulted in almost complete disappearance of the cutaneous lesions.

Incipient Darier's Disease(?); Benign Pemphigus of Hailey and Hailey(?).

M. I. M., a 2 year old white boy, was first seen here on Sept. 1, 1942, with a history of onset of "heat rash" on the scalp in June 1941, when he was 10 months of age. The eruption was characterized by vesicles and papules with crusting and scaling which spread to the regions of the axillas, groin and anus. This persisted except for a few days in July, when the patient was in the northern part of the state. Scabies was superimposed after onset. The past history is essentially irrelevant except for some wheezing soon after birth and draining ears of ten months' duration. The family history is irrelevant.

Examination revealed a red papulovesicular eruption with crusting on the scalp. A red, weeping, moist eruption was present in the axillas, groin and perianal region with some fissuring. A papulopustular, crusted eruption was present in the intrascapular area. The general examination gave normal results except for revealing bilateral external otitis media. Studies of the blood and urine and roentgen examination of the chest gave normal results, and the reactions to Kline and Kahn tests were negative. The reactions to passive transfer tests were essentially negative.

During the three weeks in the hospital the patient had a low grade fever, and on two occasions the temperature rose to 102 F. Treatment has consisted of the use of local agents, including 1 per cent gentian violet, 5 per cent scarlet red ointment, 0.5 per cent aqueous solution of acriflavine base alternating with scarlet red-oxyquinoline paste and periodic wet dressings of aluminum subacetate, and 1 per cent sulfathiazole in olive oil applied to the scalp.

DISCUSSION

DR. L. H. WINER, Minneapolis: When I saw this child on two occasions eight or ten months ago, I though he had a severe seborrheic dermatitis with involvement of the groin and scalp. The patient did not improve under the usual management of seborrheic dermatitis. The microscopic section does not resemble the histologic picture that I have of Hailey and Hailey's benign familial pemphigus. Several biopsy specimens of benign familial pemphigus have been sent from Fort Sill by Capt. L. Nelson, and they were not at all like the histologic sections seen here. I believe that a biopsy should be made of one of the lesions on the abdomen which look clinically like Darier's disease.

DR. HAMILTON MONTGOMERY, Rochester: A specimen for biopsy was taken from one of the lesions on the back that clinically looked like Darier's disease. The histologic picture is that of intraepidermal edema going to the point of vesicle formation with a benign type of dyskeratosis but without any evidence of *corps ronds* or grains. The histologic changes certainly are not those of Darier's disease and are suggestive of benign pemphigus of Hailey. The histologic picture, to my mind, represents an early phase of that disease, admitting that one usually sees more decided bullous formation in the lower layers of the epidermis. The location of the lesions in the groin and axillas and the distribution of the lesions would also fit in with the diagnosis of benign pemphigus. Frank and Rein (ARCH. DERMAT.

& SYPH. **45**:129-151 [Jan.] 1942) pointed out that not all patients with benign pemphigus have a familial history. This patient has no familial history. Goodman has repeatedly emphasized that Hailey's disease is a form of Darier's disease. In a discussion of the paper of Frank and Rein, however, Obermayer, Satenstein, Anderson, Weidman, Rein and I all felt that this condition was distinct from Darier's disease. Although the lesions on the trunk clinically suggest Darier's disease, the other lesions and the histologic picture especially make the disease in this case fit best with the condition described by Hailey as benign pemphigus.

DR. FRANCIS W. LYNCH, St. Paul: I agree with Dr. Montgomery that the section and the clinical evidence could justify a diagnosis of so-called benign pemphigus. Inasmuch as ulcers and fissures are present, the condition in this case is more severe than in others previously reported as instances of this disease.

DR. C. C. TOMLINSON, Omaha: The seborrheic character of this patient's eruption reminds me of a patient seen several years ago whose primary eruption was characteristic of seborrheic dermatitis and who later had a true pemphigus with fatal termination.

Sarcoidosis.

Mrs. G. H., a white woman aged 48, came to the clinic in November 1940, complaining of multiple small pruritic nodules on the backs of the arms and legs of five months' duration. Telangiectases were noted on the surface of the nodules, and some of the lesions presented central necrosis.

A tender node appeared in the right preauricular region two months before admission. The general health was good except for shortness of breath and a cough. The reactions to flocculation tests were negative for syphilis. A roentgenogram of the chest revealed diffuse fibrosis and an increase in the hilar shadows. A flat roentgenogram of the abdomen revealed a large spleen. Roentgenograms of the hands and feet were negative for cystic disease. The reactions to tuberculin tests with purified protein derivative in both the first and the second strength were negative.

A biopsy revealed histologic features compatible with sarcoid. Inoculation of tissue into guinea pigs and cultures of tissue for tubercle bacilli failed to reveal evidence of the organisms.

Lupus Vulgaris with Spontaneous Epitheliomatosis.

Mrs. W. M., a 59 year old Polish woman, presented herself on Oct. 27, 1938, with an extensive fungating cauliflower-like epithelioma which was superimposed on a chronic dusky erythematous dermatitis on the right cheek. The latter eruption was diagnosed as lupus vulgaris clinically and histologically. The lupus process involved the regions of the right cheek, nose, ear and neck and had been present since childhood. The epithelioma was of only two or three months' duration.

On October 28 the fungating mass was excised by electric scalpel and the base was treated by electrodesiccation. Pathologic study revealed it to be a squamous cell epithelioma, grade 2, intimately associated with tuberculosis of a hyperplastic type.

The patient was discharged on Nov. 12, 1938. She returned here four months later for a check-up. At that time the scar was healed and excellent results were noted.

DISCUSSION

DR. HENRY MICHELSON, Minneapolis: It is often stated that patients with lupus vulgaris have cancer more frequently after irradiation, but statistics show that cancer develops in unirradiated lesions almost as often as in those that have been so treated. The pathologic changes favor cancerous change.

NEW YORK DERMATOLOGICAL SOCIETY

R. H. RULISON, M.D., *President*

A. BENSON CANNON, M.D., *Secretary*

Oct. 27, 1942

A Case for Diagnosis (Pemphigus Vulgaris? Pemphigus Erythematosus?).
Presented by DR. HOWARD FOX.

F. G. N., a woman aged 69, was recently seen by me in consultation. The patient was American born, of French and Irish extraction, all of her ancestors having been gentiles, as far as she knew.

An eruption appeared for the first time, about one year ago, on the scalp. About two months later it involved the chest and groins. It appeared on the face three weeks ago. It is symmetric and profuse in the aforementioned areas. The lesions on the scalp and trunk consist of flaccid bullae and crusts. On the nose and cheeks, there are red, diffuse areas which suggest the appearance of lupus erythematosus. The patient complains of severe itching, but no scratch marks are present. She shows a decided Nikolsky sign. The mucous membranes of the mouth are not affected. Her general health is excellent, and she has not lost any weight.

Previous treatment has consisted of administration of vitamin B_1, liver and iron.

DISCUSSION

DR. A. BENSON CANNON: The location of the lesions on the face reminds one of lupus erythematosus, especially when the patient is viewed from a distance, but the character of the exudative process on the face in no way suggests that diagnosis. Furthermore, the lesions on the body and extremities are characteristic of pemphigus vulgaris, and I have no doubt that they will run the rapid course of a true pemphigus rather than that of pemphigus erythematosus.

DR. FRED WISE: This eruption corresponds in every essential detail with the Senear-Usher syndrome as described by those authors. My experience has been different from that of Dr. Cannon with respect to the lupus-erythematosus-like aspect of the facial eruption. In the few cases in which tissue from the face has been examined histologically, the lesions simulating lupus erythematosus have not shown the changes peculiar to that disease. In my opinion, which I expressed many years ago, the disease in cases of this kind is a variety of pemphigus vulgaris, and in some of them the fatal type of pemphigus develops as the months or years go on.

DR. HOWARD FOX: May I ask the discussers to mention their experience with the Nikolsky sign in the Senear-Usher type of pemphigus?

DR. FRED WISE: I believe the Nikolsky sign during certain stages of development is just as common in this disease as in pemphigus vulgaris.

DR. A. BENSON CANNON: My experience with pemphigus erythematosus is different from that of Dr. Wise. I feel that the Senear-Usher type of pemphigus is more benign than that of pemphigus vulgaris and that one rarely finds a Nikolsky sign. I believe that this sign can be demonstrated in conditions other than pemphigus. Some time before Senear and Usher published their report on pemphigus erythematosus, Dr. Senear wrote me that I had presented a patient with symptoms characteristic of the disease before the New York Academy of Medicine. In this patient's case the question of diagnosis rested between pemphigus and lupus erythematosus.

DR. GEORGE M. MACKEE: I have the opinion as expressed by Dr. Wise that eruptions which resemble both lupus erythematosus and pemphigus represent a variety of pemphigus rather than lupus erythematosus—pemphigus erythematosus. Some or most of them run a benign course, but the prognosis should be guarded.

What has confused me is clinical lupus erythematosus with an occasional bulla or area of exudation. At present I am inclined to think that there are both pemphigus erythematosus and lupus erythematosus bullosus, which have to be differentiated.

DR. FRANK C. COMBES: If this patient did not have lesions on the body I do not think any one would hesitate to make a diagnosis of lupus erythematosus, based on the lesions on her face. There is often this problem of differentiation between lupus erythematosus bullosus, pemphigus vulgaris and pemphigus erythematosus. I do not think at this time it can be definitely decided on. In his presentation Dr. Fox mentioned that this patient had had no loss of weight. In my experience I do not think loss of weight is particularly significant with pemphigus vulgaris. Late in the disease, just before a patient dies, he will lose weight rapidly, but I have seen patients with extensive pemphigus vulgaris who have even gained weight.

DR. GEORGE C. ANDREWS: I do not understand the point of conflict between Dr. Wise and Dr. Cannon. It seems to me that they say the same thing except as to the prognosis.

DR. A. BENSON CANNON: I did say that this case was one of pemphigus. I believe that the lesions in the Senear-Usher type of pemphigus would be more typical of lupus erythematosus. I have never seen lupus erythematosus with edematous, crusted, oozing lesions.

DR. PAUL E. BECHET: In my opinion the confusion in the differential diagnosis between the Senear-Usher syndrome and lupus erythematosus bullosus is mostly due to the fact that the former not infrequently appears on the favorite sites of discoid lupus erythematosus, namely, the forehead, cheeks, nose and upper part of the chest and back, and may remain there for a year or more before its inevitable extension to other parts of the body. Other points of apparent similarity between the two dermatoses are their discoid appearance and the scaling. However, in the Senear-Usher syndrome the lesions are larger and the scales are moist and easily lifted, leaving a moist reddened surface. What few bullae may be present are almost invariably flaccid and almost flattened. It is my belief that bullous lupus erythematosus is a great rarity. I strongly suspect that in the few cases reported the disease developed later into the Senear-Usher syndrome, which in my opinion is a mild pemphigus of slow development. As this syndrome invariably becomes worse in time, not infrequently developing into a severe fatal pemphigus, I believe the word mild or benign should not be used in its description.

DR. J. FRANK FRASER: The duration of one year without signs or symptoms of illness and the fact that there are no lesions of the mucous membranes speak against the diagnosis of pemphigus vulgaris.

DR. PAUL E. BECHET: Lesions of the mucous membrane may or may not be present in the Senear-Usher type of pemphigus.

DR. FRED WISE: I have observed perhaps 3 cases of lupus erythematosus in which there were bullae forming part of the eruption.

DR. FRANK C. COMBES: I believe Norman Walker said he was unable to differentiate lupus erythematosus bullosus from erythema multiforme bullosum.

DR. GEORGE M. MACKEE: Lupus erythematosus is rarely associated with bullae. It is more common to see edema, exudation or a nodule. The difference between the bulla and the nodule is possibly due to the location of the fluid. If superficial, it may cause a bulla; if deeper, it may cause a nodule or an area of edema.

DR. HOWARD FOX: I am firmly convinced that this patient is suffering from some variety of pemphigus. Dr. Senear and the Chicago dermatologists who are especially interested in this disease are convinced that the disease now called pemphigus erythematosus has nothing to do with lupus erythematosus. It is simply a variety of pemphigus. I felt that the most likely diagnosis in this case was the erythematosus and not the vulgaris type of pemphigus, because the patient had no lesions in the mouth and was not sick. She has had no constitutional symptoms

at any time. I was a little surprised at the extreme edema of the skin, as shown by the Nikolsky sign. This disease is certainly more benign than pemphigus vulgaris, but I was under the impression that there was not as pronounced a Nikolsky sign as this woman shows. Dr. Bechet spoke of pemphigus erythematosus as an entity. I should say it is a variety of pemphigus, of a relatively benign type, although in some patients pemphigus vulgaris eventually develops and they die of it. Finally, I should like to mention the loss of weight discussed by Dr. Combes. It has been my experience that this may occur early in the disease. Later, when patients have bullae in the mouth and cannot eat properly, they lose weight, but I have seen patients with a loss of 20 pounds (9 Kg.) or more early in the process, when it was not due to soreness of the mouth or lack of nourishment. Often, after the initial loss of weight they regain their weight, at least temporarily.

DR. PAUL E. BECHET: Dr. Fox is correct. When I inadvertently stated that the Senear-Usher syndrome was an entity, I meant to say that this syndrome presents a definite, similar clinical picture in the majority of cases and that it is true pemphigus, no matter how mild its appearance.

Knuckle Pads. Presented by DR. R. H. RULISON.

D. R., a youth aged 17, the son of a physician, was first seen in October 1937, because of thickening of the skin with some increase in the folds and a faint yellowish color in the knuckle area (over the metacarpophalangeal joint) of each index finger. The eruption had been present for one year at the first examination. It was more pronounced on the right knuckle than on the left. No cause for this thickening was discovered. Salicylic acid thinned the skin, but the disease was not cured.

The patient returned on April 15, 1942. At this time, thickened, yellowish areas were present over several knuckles of both hands. Dr. Howard Fox saw the patient with me and suggested that, although the disease is usually resistant to treatment, a few doses of roentgen rays might possibly be tried.

On May 4 the patient was given 350 r, unfiltered, to the thickened areas over the knuckles of the index and little fingers of the left hand (there were no abnormalities of the intervening two knuckles). On May 13 another unfiltered dose of 300 r was given. On May 20, 300 r, filtered through 1 mm. of aluminum, was given. On May 27 there was a moderate reaction. This was subsiding over the knuckle of the little finger but was still present over the knuckle of the index finger. On June 8 the reaction had disappeared. There was no improvement from treatment, but slight pigmentation over the treated area of the knuckle of the index finger was present. The right hand was not treated. No further treatment has been given.

In looking up the literature on knuckle pads I found that the lesions are usually located over the proximal interphalangeal joints. In this case the skin over the metacarpophalangeal joints is affected.

DISCUSSION

DR. FRANK C. COMBES: I agree with the diagnosis. Conditions like this are not due to trauma.

DR. GEORGE M. MACKEE: I agree with the diagnosis of knuckle pads. I have never been able to ascertain the cause, nor have I had therapeutic success with various remedies and methods.

DR. FRED WISE: I agree with what Dr. MacKee has just said, but I have an idea that persistent use of solid carbon dioxide should bring about amelioration, if not cure. I know that roentgen treatment is useless. I have tried it. I should continue to use solid carbon dioxide and see what happens.

DR. A. BENSON CANNON: I suggest that the treatment consist of application of elastoplast over each of the knuckle pads, its removal after ten days or two weeks, cleansing of the area with ether and another application of elastoplast.

With this treatment I believe that the lesions would heal in a few weeks. One could use adhesive plaster, but it does not stay on as well as the elastoplast. The protection and immobilization of the skin over the affected parts are important factors in the treatment. One may wash the hands with soap and water without disturbing the elastoplast.

DR. GEORGE M. MACKEE: Dr. Cannon, did you get any clue as to the cause?

DR. A. BENSON CANNON: Knuckle pads are probably the result of an irritative process bringing about pathologic changes in the skin comparable to those found in neurodermatitis. Trauma or some external irritation often is responsible for knuckle pads. I have cured several patients with elastoplast.

DR. GEORGE M. MACKEE: One of my patients had the habit of rubbing the knuckles, but there was no history of repeated traumatism or irritation in my other patients. I have never used Dr. Cannon's method of protection, but I have employed salicylic acid plaster without harm or benefit.

DR. R. H. RULISON: This boy does not have any habit of fussing with his hands and has not been engaged in any activity which would cause this. Trauma is therefore out of the question. I looked up the literature on this subject. An English author named White showed a photomicrograph of this process. There is hypertrophy of the corium. The papillae show no alteration, which, he says, excludes the possibility of a corn. The corium is normal, but in it there is a poorly nucleated vascular tissue constituting a tumor. There is no evidence of inflammation, and the reaction does not suggest an ordinary fibroma. That was as much of a pathologic picture as I could get. The process is located apparently at the bottom of the corium and extends deeper than that. The interesting thing about this is that in some cases the condition is later associated with Dupuytren's contracture and in some it is hereditary. There is nothing in this boy's history to suggest either of those. Most of the lesions reported in the literature are located over the proximal interphalangeal joints and not over the metacarpophalangeal joints as in this case. Practically all of the published illustrations show the lesions in the former location.

Sarcoma of Kaposi with Buccal Lesion. Presented by DR. FRED WISE.

B. H., a man aged 65, presented from the New York Skin and Cancer Hospital, first observed small purplish red flat nodules on the backs of his hands ten years ago. Shortly after, similar lesions appeared on the forearms, extending from the hands to the region around the elbows, and then on the dorsa of the feet and the anterior surfaces of the legs, from the ankles to the knees. In recent months, a group of dime-sized plaques which have undergone ulceration have appeared on the palms.

Examination discloses a large number of pea-sized to hazelnut-sized tumors on both forearms, much more numerous on the right than on the left. The right palm is the site of four ulcerated and infiltrated plaques, with sharp margins. The lesions on the forearms display many different stages of evolution, from old ones to those appearing only within the past few months. On the legs the eruption has undergone partial involution following roentgen treatment, leaving the surface with a dry, edematous and ichthyotic skin. On the posterior aspect of the hard palate there is an elongated, purplish red plaque, about 25 by 5 mm. in size, situated transversely across the roof of the mouth. The patient is not aware of its presence.

The patient appears to be well nourished and does not complain of disturbances other than his eruption and the pain caused by the ulcers on the right palm.

DISCUSSION

DR. GEORGE M. MACKEE: An interesting feature of this case is the lesion on the hard palate, which indicates, as is well known, that there is hardly any part of the body exempt from this disease.

DR. HOWARD FOX: One unusual feature in this case is the lesion on the palate, but another unusual feature is the ulceration. Kaposi's sarcoma is characterized by lack of ulceration and the small size of the lesions. Large tumors do not occur, as in mycosis fungoides. I saw this patient previously in consultation and advised roentgen treatment to the limit of toleration. This apparently helped him for a while, and I do not know why it was not continued.

DR. J. FRANK FRASER: The question of the nature of Kaposi's sarcoma has never been satisfactorily settled. The English pathologists hold the view that the process is inflammatory and that the development of sarcoma is coincidental. Lang and Haslhofer concluded that the disease is a generalized angiomatosis (Lang, F. J., and Haslhofer, L.: Ueber die Auffassung der Kaposischen Krankheit als systematisierte Angiomatosis, *Ztschr. f. Krebsforsch.* **42**:68, 1935). Observations in 1 of my own cases seemed to lend support to that view. The early lesions in this case showed identical features with those seen in Dr. Wise's case. I used roentgen therapy without beneficial results. The cutaneous lesions grew larger and assumed the characteristic appearance of deep-seated angiomas. New lesions developed in the lungs and other visceral organs. Whether the spread was by metastasis or of multiple primary origin was not determined. Necropsy was not permitted. My own belief leans toward the multiple primary theory, but it must be remembered that cavernous angiomas do occasionally form metastases in the lungs (Boyd, W.: A Text-Book of Pathology, ed. 2, Philadelphia, Lea & Febiger, 1934, p. 310).

DR. GEORGE C. ANDREWS: Was there not spindle cell sarcoma in some of the early cases?

DR. J. FRANK FRASER: The histologic picture in the cases of Kaposi's disease as it is known today is not the same as that described in Kaposi's original article as round cell sarcoma. I have seen the picture of fibroblastic sarcoma in these lesions, but round cell sarcoma never.

DR. GEORGE C. ANDREWS: One of my patients died of spindle cell sarcoma.

Poikilodermatomyositis (Lupus Erythematosus Disseminatus?). Presented by DR. EUGENE F. TRAUB.

T. L., a woman aged 45, came to the New York Skin and Cancer Hospital on Sept. 14, 1942 because of a generalized eruption of seven months' duration. In February 1942 the patient noted an eruption on the back of the neck. Then the eruption progressed to involve the extensor surfaces of the arms and forearms as well as the V area of the chest. It consisted of roughness and redness of the skin and was itchy. Her family physician advised consultation with a dermatologist, who said that she had an eruption due to a plant. She disposed of a plant (pandanus?) which had been in her house for twelve years. He also advised intravenous injections of calcium gluconate, of which she was given twenty. The eruption did not improve. The face, back and thighs became involved. She then consulted another dermatologist, who gave her roentgen treatments for ten weeks. On Tuesdays he treated the face, chest and back, and on Fridays, the legs and arms. He also prescribed lotions and ointments. The roentgen treatments stopped the pruritus. However, she began to break out in sores on the back, arms, forearms and hands. These sores were covered with small gritty particles like sand or salt. Pains developed in the shoulders, elbows and hands. About the middle of August 1942 she consulted an internist for treatment of the arthritis. He prescribed capsules and three medical diathermy treatments to the arms, forearms and hands. These treatments relieved the pains in the joints. Since the eruption was not clearing, she consulted me on Sept. 14, 1942 and was hospitalized.

The patient had pleurisy in 1924 and inflammatory rheumatism in 1925. In 1933 she had a nervous breakdown, and she took "nerve medicines" and "ovarian extracts" for three years at that time. Since 1933 her menstrual periods have

become less regular and the flow has been scanty. She has three children living and well, the youngest being 4 years old. There has been no history of excessive exposure to the sun.

Physical examination shows a slightly obese woman with an erythematous eruption involving the whole face, the neck, the upper parts of the chest and back, the shoulders, the arms and the dorsa of the hands, the thighs, the hips and the knees. There is slight scaling. The entire skin in these areas is thin and presents a peculiar wrinkling, many areas of definite atrophy and minute telangiectases. The wrinkling of the skin is particularly well shown on the sides and front of the neck and on the upper part of the back. The minute telangiectases can be seen better on the sides of the neck, where there is also a faint reticulated hyperpigmentation. The whole face is a little swollen. The eyelids show a definite puffiness with distinct small telangiectases. The extensor surfaces of the arms and forearms show a certain hardness, as in scleroderma. On the dorsa of the hands and of the fingers, the skin is thin and erythematous. The palms are completely spared. There are no lesions below the knees.

On the upper part of the chest and on the back are many areas of scarlike atrophy, especially a few irregular areas in the middle of the back. At the lower border of the eruption, on the breasts and on the back, are many excoriations with adherent scales and erythematous halos. Similar lesions are seen on the flexure surfaces of the forearms and on the hips and thighs. Two larger lesions of the same nature are present on the inner aspect of the right knee. All these lesions are painful. They look like papulonecrotic or maculonecrotic lesions of the skin.

The muscular strength of the fingers seems to be diminished. There is no pain on pressure of the muscles. There is pain on pressure of the skin where there are necrotic lesions. There are a few small subcutaneous calcifications on the right arm, just above the cubital fold. There is a less well pronounced eruption on the middle of the abdomen. There is leukoplakia of the buccal mucosa, especially opposite the upper teeth in the back. There is a network-like appearance on the right buccal mucosa and on the inner surface of the lips. The results of medical and neurologic examinations were negative.

Two weeks after admission to the hospital the necrotic-like lesions on the breasts and on the back had healed. Also, a large erythematous plaque on the back had become fainter in color. Fresh necrotic lesions had appeared on the abdomen and on the thighs. The lesions on the inner aspects of the knees were healing.

The blood count showed 4,560,000 erythrocytes and 7,600 leukocytes, with a differential count of 62 per cent polymorphonuclear neutrophils, 8 per cent eosinophils, 21 per cent lymphocytes and 9 per cent monocytes, and 220,000 platelets. There was 82 per cent hemoglobin. The bleeding time was three minutes and the coagulation time one minute. The urine was normal on six occasions, with densities of 1.004, 1.008, 1.010, 1.018 and 1.008. The sedimentation rate of the blood was 19 mm. in one hour. The icteric index was 5.3 units. The Wassermann and Kahn reactions of the blood were negative. The reaction to a Hanger cephalin flocculation test was 4 plus. The prothrombin clotting time was twenty-one seconds. Clot retraction was complete in four hours. The vitamin C level in the blood was 1.2 mg. per hundred cubic centimeters and the vitamin C saturation test showed 620 mg. in five hours. Chemical examination of the blood showed 8.5 mg. of urea nitrogen per hundred cubic centimeters, 26 mg. of nonprotein nitrogen, 1 mg. of creatinine, 4.8 mg. of creatine, 85 mg. of dextrose, 3.6 mg. of inorganic phosphate, 13.4 mg. of total calcium and 6.3 mg. of ionized calcium; the ratio of urea nitrogen to nonprotein nitrogen was 32 per cent; there were 5.6 units phosphatase activity, 7.9 per cent total proteins, 3.6 per cent globulin, 4.3 per cent albumin, with a 1.2 ratio of albumin to globulin, and 275 mg. of cholesterol per hundred cubic centimeters.

The basal metabolic rate was 10 per cent above normal. The Sulkowitch test of the urine showed a moderate amount of calcium excreted. Porphyrins

in the urine were less than 100 Gm. in twenty-four hours. The creatinine in the urine was 2.084 Gm. in twenty-four hours and the creatine 0.137 Gm. The 17-keto steroids in the urine amounted to 6.2 mg. in twenty-four hours. An electrocardiogram showed a left axis deviation, which might be due to the position of the heart in the chest (Dr. J. S. Butterworth). An electroencephalogram showed no abnormal electrocortical activity (Dr. Bernard L. Pacella). Roentgenograms of the arms, forearms, hands and thighs were normal except for fibrous thickening in both thighs in the upper portions.

Histologic examination of the skin showed an atrophic epidermis containing irregularities and swellings of the basal cells and a nonparakeratotic scale. There was a large amount of edema in the upper part of the corium. The blood vessels seemed increased in number and often were surrounded by a cellular exudate consisting of lymphocytes. Occasional cells containing a brownish pigment were present. The collagen fibers below the edematous zone showed a decided granular degeneration. Even in the edematous zone where the collagen fibers were present there was that tendency toward granular degeneration. The elastic tissue stain showed an absence of fine elastic tissue fibers except in one area, where they still persisted but in a swollen state. The calcium stain showed small nests of dark blue-staining spicules high up in the corium. These were usually associated with the presence of cells. The histologic diagnosis was lupus erythematosus with roentgen ray changes.

Histologic examination of a specimen of muscle showed nothing of great importance except toxic changes. The stain for calcium was negative.

The therapeutic test with prostigmine (by Dr. Maurice Bruger) showed the following results: Before prostigmine, the values for urinary creatinine and creatine, urinary creatinine and urinary creatine, were respectively: on October 5, 2.02 Gm., 1.85 Gm. and 0.170 Gm.; on October 6, 2.13 Gm., 1.94 Gm. and 0.19 Gm.; on October 7, 2 Gm., 1.74 Gm. and 0.26 m. After prostigmine, 15 mg. three times a day, these values were respectively: on October 15, 2.84 Gm., 2.76 Gm. and 0.08 Gm.; on October 16, 2.7 Gm., 2.42 Gm. and 0.28 Gm.; on October 17, 2.69 Gm., 2.57 Gm. and 0.12 Gm. The average creatine in the twenty-four hour specimen of urine was 206 mg. before the administration of prostigmine and 160 mg. afterward.

DISCUSSION

Dr. A. Benson Cannon: I could see the poikiloderma-like changes in the skin but could find no evidence of a dermatomyositis. I think that the lesions in this patient are confined to the skin, and I regard the case as being one of poikiloderma rather than of poikilodermatomyositis. In some respects the affected parts resemble lesions of disseminated lupus erythematosus, acrodermatitis chronica atrophicans or a scleroderma-like process. I sometimes wonder if there is not a common origin in these inflammatory processes of the skin ending in atrophy that may be traceable to an endocrine disturbance.

Dr. Fred Wise: I think that the most probable diagnosis is the one that has been offered by the presenter. The muscle tissue did not show the changes that one expects in dermatomyositis, but I believe that a single biopsy cannot be depended on because the biopsy specimen had not been taken from the affected muscle or the changes were so meager that they did not show enough to demonstrate the myositic changes which occur in this disease.

Dr. George M. MacKee: I accept the diagnosis of poikiloderma because of atrophy, scaling and telangiectasia, in other words, the appearance of chronic radiodermatitis, but I do not think the myositis has yet been definitely proved.

Dr. Howard Fox: I agree entirely with Dr. MacKee. Clinically, if this woman has a generalized myositis, she ought to have a good deal of tenderness. She has none at all. I think the term poikiloderma covers the ground without addition of the term myositis. Certainly this case was not like the one which Dr. Hopkins presented last year.

DR. GEORGE C. ANDREWS: The patient does not have fever now and has no tenderness in the muscles; nevertheless, if those muscles of the upper extremity were tested electrically, there might be some signs of muscular degeneration and weakness of the muscle groups. The excessive amount of creatine in the urine would indicate an increase in muscle metabolism and destruction of muscle tissue. Of course the increase in creatine is not enormous, but several tests were made and it is suggestive. Although the presenter has not proved that the patient has a myositis, it is likely that she has, and I agree with the diagnosis of poikilodermatomyositis.

DR. GEORGES LECLERC (by invitation): I admit that this patient does not yet show much muscular involvement. She has had the disease only seven months, and it is a chronic entity which may last for many years. If observed at a later stage, she may show these muscle changes. The only finding suggestive of myositis is the high creatine content of the urine. There is not much evidence in the literature on these creatine figures in this disease, and even in Bodansky's book (Bodansky, M., and Bodansky, O.: Biochemistry of Disease, New York, The Macmillan Company, 1940) there are only ten lines discussing this disease, dermatomyositis, out of twenty pages on diseases of muscle. It is not the creatinine that is important here but the creatine. The creatinine in the urine varies from day to day with the ingestion of protein, while the creatine is the result of muscle metabolism. It is mentioned in the literature that most of the cases of dermatomyositis have been described by the neurologists and the description of the cutaneous changes is scanty, while most cases of poikiloderma have been described by dermatologists and investigation into the muscle changes has been scanty. Therefore, it is not known whether the former cases were really instances of poikilodermatomyositis or the latter of true poikilodermatomyositis.

DR. GEORGE C. ANDREWS: May I add that in the case of poikilodermatomyositis which I presented here last year, the creatine in the urine amounted to 480 mg.? All of the members agreed with the diagnosis. The patient had weakness in some muscle groups and a history of tenderness at times in different muscle areas. She had a rise in temperature of 1 or 2 degrees. She is still alive and still has the disease.

DR. GEORGES LECLERC (by invitation): One case has been reported in which there was a creatine content of 1,100 mg.

Extensive Roentgen Ray Dermatitis; Epitheliomas; Results of Therapy.
Presented by DR. A. BENSON CANNON.

Miss J. C., aged 60, a school teacher, consulted me in April 1942 for treatment of extensive roentgen ray dermatitis and for removal of two epitheliomas in the injured area of the right cheek. She stated that she had had roentgen treatment for acne twenty-five to thirty years previously, the exact number and amount of treatments not being known. Five to eight years after the treatments she noticed the first evidence of injury with the formation of bluish red spots on her face. The damage grew worse, and numerous brown areas and white scars appeared. Ten to twelve years after the roentgen treatments she consulted a dermatologist, who treated the most severely affected areas with radium and prescribed a salve. The radium made the condition worse and produced an ulceration of the skin in two areas, which had to be removed by surgical excision. Since that time she has had two other operations for removal of cutaneous cancers, the last operation a year ago. Painful sore spots would appear on the sides of the face from time to time, for which she applied cod liver oil. Histologic study of each ulcer removed showed epithelioma.

Examination showed an extensive roentgen ray dermatitis on both sides of the face, the neck and the lips, the right side of the face being most severely affected. Hard scarred areas studded with pea-sized to dime-sized, brown, some macular and other papular and keratotic, telangiectatic, angiomatous papules and a few

pea-sized, red keratotic papules were present. On the right cheek there were two pea-sized to dime-sized, red, granular, warty, ulcerated, crusted areas, the edges being exceedingly hard, pearly and telangiectatic. Histologic study of tissue removed from two ulcers showed basal cell epitheliomas.

Treatment consisted of removal by desiccation and curettage of the two epitheliomas and desiccation of the telangiectatic, pigmented, elevated, scarred areas on the right side of the face, chin and neck, leaving the left side to compare with the treated areas on the right side.

The case is presented to show the results of this treatment.

DISCUSSION

Dr. George C. Andrews: That was a nice result, and I think it is agreed that electrodesiccation is a good treatment in many cases of chronic roentgen ray dermatitis and small epitheliomas. However, I have been astonished and distressed a few times to find that chronic radiodermatitis and epitheliomas are not as simple to get rid of or to cure as one might be led to expect. It is true that one may be able to handle the majority of lesions by this simple method, but one never knows which lesion will not respond to this treatment and will get out of hand and cause irreparable damage and perhaps death. Therefore, I do not think that this treatment can be accepted as the general rule.

Dr. Howard Fox: I think it is agreed that a good cosmetic result was obtained in this case. Dr. Cannon said that two of these lesions showed basal cell epithelioma. I was under the impression that epitheliomas following radiodermatitis were, as a rule, of the squamous cell type.

Dr. George M. MacKee: There is a definite esthetic improvement in the treated side of the face. However, I feel that the skin on the treated side is still a menace to this patient and always will be. As far as epithelioma is concerned, the usual type is squamous cell, but basal cell epitheliomas and basosquamous neoplasms may occur. Rarely the so-called spindle cell epithelioma is encountered. These are difficult to cure, and as a rule a wide deep excision is required because it is impossible to determine, either clinically or histologically, where the pathologic tissue begins or ends. Such an operation must be followed by plastic repair.

Dr. Fred Wise: Dr. Cannon should be congratulated on this result. This method of treatment is useful when superficial structures are involved but not in cases in which deeper structures are affected. The use of emollient creams persistently applied to that skin and the avoidance of sunlight will keep this woman's face in good condition for the rest of her life.

Dr. A. Benson Cannon: I had always thought that epitheliomas occurring as a result of postradiation changes were usually of the squamous cell type, but I have found the reverse to be true. Usually four out of five epitheliomas that I have removed from areas of radiodermatitis have been reported by the pathologist as basal cell. My experience has been that the sooner the epithelioma appears after a radiation injury the more likely the growth is to be of a squamous cell variety, the more rapid the growth and the more difficult to cure. On the other hand, epitheliomas occurring ten to fifteen years after postradiation changes are apt to be basal cell and most benign. I have often been agreeably surprised at the excellent results I have obtained in the removal of apparently inoperable epithelioma occurring in postradiation injured skin by means of electrodesiccation and electrocoagulation. Some two years ago I took an epithelioma off the skin of the upper lip in an old radiodermatitis, and at operation I found that the diseased tissue burrowed well down underneath the skin and into the vermilion border of the lip. Thorough electrocoagulation plus curettage resulted in a beautiful cosmetic cure that has lasted for two years. I have found that most epitheliomas in scar tissue are relatively benign.

DR. GEORGE C. ANDREWS: To illustrate what I mean, a boy came to the office about a year ago because he had a "pimple" on the chin for about three weeks. He had had roentgen treatment from some other physician for acne. I saw that the lesion was not a pimple. It looked like an epithelioma. A biopsy showed basal cell epithelioma. A week later with the area under procaine hydrochloride anesthesia I cut it out thoroughly with the electric cutting current. He was to return in two weeks for dressing, but he lived far away and failed to come in. He returned a month later. The growth had infiltrated the deeper tissues and become extremely serious. I think that at that time he also saw Dr. MacKee. We both decided that he should go to Dr. Pack, who operated and removed most of the chin, resected the gums and the periosteum of the mandible. That was an infiltrating basal cell epithelioma. Dr. Pack looked at the sections in my presence and could find no spindle cells. From the course, the spindle cell type was expected but it was not this type.

Xanthoma Tuberosum Coincident with Psoriasis, with Xanthomatosis of the Coronary Vessels. Presented by DR. FRED WISE.

S. B., a man aged 34, registered at the New York Skin and Cancer Hospital on Aug. 4, 1942, presenting yellowish lesions on the trunk, palms and elbows of sixteen months' duration. His father had psoriasis and arthritis. The patient has been under the care of the hospital for generalized psoriasis since the age of 3 years. His general health has been good except for bleeding gums in 1937. He has been accustomed to eat fried and greasy foods and a great deal of bread and butter. About three months ago he had a "heart attack," and he has been hospitalized for six weeks. There are no other subjective symptoms.

The xanthomatous lesions began as pea-sized growths on the dorsal surfaces of the base of the right middle finger and the middle joint of the left index finger. During the past sixteen months they began to develop on the palmar surfaces of the fingers, the hands and the extensor surfaces of the elbows. His average weight has been between 189 and 193 pounds (86 to 88 Kg.). His weight now is 150 pounds (68 Kg.). He has been prescribed an 800 calory, low fat and low cholesterol diet. Most of the psoriatic and xanthomatous lesions have been regressing fairly rapidly as a result of this diet program. He looks older than his age. His face is ashen color.

The eruption consists of generalized lesions on the scalp, trunk and limbs. On the scalp and eyebrows are several small seborrheic crusted patches. On the trunk and extremities, most numerous on the back, are many discrete pea-sized and somewhat larger reddish patches mostly with denuded surfaces but with peripheral psoriatic scaling. On the extensor surfaces of the elbows are raised yellow plaques 4 by 4 cm. in size. The anterior border of the plaque on the right elbow is purplish red and is covered with fine silvery dry scales. On both palms and over the interphalangeal joints and the heads of the metacarpals are yellowish, flattened, somewhat raised xanthomatous growths and bands.

The hemograms were normal except for 12 stab cells (normal, 3 to 5 per cent of the total white cells) on August 11 and an erythrocyte count of 6,170,000 and 17.5 Gm. of hemoglobin per hundred cubic centimeters of blood (105 per cent) on August 27. The chemical examination of the blood plasma on August 3 showed 0.4 Gm. of fibrinogen (normal, 0.2 to 0.3 Gm.). Examination of the blood serum on August 11 for proteins and lipids gave the following results: total proteins 6 Gm. (normal, 6 to 8 Gm.), albumin 3 Gm. (normal, 4 to 5 Gm.), globulin 3 Gm. (normal, 2 to 3 Gm.), ratio of albumin to globulin 1:1 (normal, 1.6 to 2.0:1), total lipids 810 mg. (normal, 500 to 700 mg.), fatty acids 470 mg. (normal, 200 to 420 mg.), cholesterol 335 mg. (normal, 160 to 230 mg.) and cholesterol esters 175 mg. (normal, 100 to 150 mg.). On August 28 the total cholesterol was 360 mg., cholesterol esters 220 mg. and the ratio of cholesterol

esters to total cholesterol 61 per cent (normal, 40 to 60 per cent). On September 14 the total cholesterol was 300 mg., cholesterol esters 160 mg. and the ratio of esters to total cholesterol 53 per cent.

The results of determination of vitamin C (ascorbic acid) in the blood plasma and the Hanger cephalin-cholesterol flocculation tests were normal. The sedimentation rate was 17 mm. per hour on August 3 and 22 mm. on September 5 (normal male, 10 mm. per hour by the Westergren method). The report of the icteric index on August 27 stated that "the color match was impossible, the serum being too lipemic." Electrocardiographic studies showed evidence of posterior myocardial infarction.

A section was taken from the elbow and examined by Dr. Charles F. Sims. He diagnosed it as xanthoma and described it as follows: "The epidermis was irregular and covered in part with a thin horny layer. The granular layer was present throughout the section. Some of the rete pegs were elongated and narrow; others were broad. In the midcutis were several ill defined areas composed of numerous fat droplets within the cytoplasm of the foam cells. The vessels of the upper part of the cutis and midcutis were moderately dilated and surrounded by a sparse cellular infiltration composed of small round cells and occasionally wandering connective tissue cells. There was a moderate interstitial and parenchymatous edema of the upper and middle parts of the cutis."

DISCUSSION

DR. AUSTIN W. CHEEVER (by invitation), Boston: I have never seen these two diseases together before. I do not think they have any relation to each other, but both happen to have occurred in the same patient at the same time.

Pityriasis Versicolor (with Unusually Extensive Involvement). Presented by DR. FRANK C. COMBES.

A. B., a girl aged 16, came to the clinic at Bellevue Hospital yesterday with a dermatosis of four years' duration. It began on her chest and continued to spread notwithstanding the application of various remedies.

The disease is typical but particularly extensive. The entire trunk is involved. Large areas are present in each cubital fossa and guttate and nummular patches cover both thighs. The involved areas are lighter in color than the normal skin, suggesting the picture described by Pardo-Castello and Dominguez as "achromia parasitaria" (Pardo-Castello, V., and Dominguez, M.: Achromia Parasitaria. ARCH. DERMAT. & SYPH. **9**:82 [Jan.] 1924).

Scrapings from the pale areas showed an abundance of Microsporon furfur.

DISCUSSION

The members were in unanimous agreement with the diagnosis as presented.

Necrobiosis Lipoidica Diabeticorum Without Diabetes. Presented by DR. FRED WISE.

S. D., a woman aged 26, presented for Dr. Jack Wolf, registered at the New York Skin and Cancer Hospital on Oct. 26, 1942, presenting lesions on her legs of two years' duration. Her hands and feet are "always cold." She has otherwise been in good health.

The present eruption began when she bruised her knees and legs in an accident. She said that the lesions appeared almost immediately and that they all came out at the same time. They have never undergone regression. There are no subjective symptoms, but the lesions are painful when she "bumps" them. She has not received any treatment but has exposed her legs to the sun frequently.

There are several shiny reddish yellow nontender plaques on the extensor surfaces of both legs. They are well defined, rounded and oval. There are

three patches on the right leg varying in size from 2 to 4 cm. and five on the left leg, the smallest of which is pinhead sized while the largest is 4 by 10 cm. Three small patches on the left leg are of a dull reddish color. Two lesions on the upper third of the left leg show a lighter central zone with a slightly raised border. Their color disappears only partially on moderate diascopic pressure, disclosing yellowish stains.

Tests of the blood and urine gave normal results. A histologic section removed from a lesion on the leg was examined by Dr. Charles F. Sims and diagnosed as necrobiosis lipoidica. The description is as follows: The epidermis was thinned, with the rete pegs flattened for the most part. In the upper and middle parts of the cutis and in parts of the section in the deep portion of the cutis there was a focal and diffuse cellular infiltration composed for the most part of small round cells, some wandering connective tissue cells and occasional plasma cells. However, foreign body giant cells and epithelioid cells were present in some of the infiltrated areas in the upper part of the cutis. In these areas the collagen appeared fragmented and granular with some basophilic strands. With sudan III numerous fine fat droplets could be noted within the infiltrated zones. In the latter the elastic tissue was absent. The capillaries of the subepidermal zone were dilated. The blood vessels throughout the cutis were dilated, their walls edematous and in some instances torn, whereas in some there was an endothelial proliferation causing almost complete obliteration of their lumens.

DISCUSSION

DR. AUSTIN W. CHEEVER (by invitation), Boston: I do not see why the term "diabeticorum" should not be dropped entirely. At the Massachusetts General Hospital in more than half of the cases of this disease diabetes does not develop, even after a considerable time. Just because this did occur in the early described cases, I do not see why the term "diabeticorum" should be retained.

DR. FRANK C. COMBES: I agree with Dr. Cheever, but this term must continue to be used because it is in the Standard Nomenclature of Disease.

DR. HOWARD FOX: Necrobiosis lipoidica diabeticorum is the title the committee on nomenclature chose for inclusion in the Standard Nomenclature of Diseases. It was thought that the majority of these patients did have diabetes eventually, if not at the time of examination.

DR. FRED WISE: In the opinion of the European dermatologists, all patients with lesions like those affecting this patient are candidates for diabetes, even after many years.

Sarcoid of Boeck. Presented by DR. FRED WISE.

A. McC., a white woman aged 53, registered at the New York Skin and Cancer Hospital on July 30, 1942, presenting lesions on the hands of ten months' duration. The family history is irrelevant. She had one stillborn infant and one infant who lived for five days. She has a son aged 21 who is healthy. The patient does not recall having any diseases of the skin or other ailments. During the past five months she has had a lack of appetite and has lost about 12 pounds (5.4 Kg.). There are no subjective complaints.

The present illness began with a "red rash and little pimples, which appeared suddenly, overnight. The rash disappeared, leaving a reddened surface, which gradually became hard and swollen."

The lesions are located on the anterior half of the dorsal surfaces of the hands, the proximal and middle phalanges of the ring, middle and little fingers of the right hand and the anterior outer third of the dorsal surface and the proximal phalanges of the index and middle fingers of the left hand. They are raised in the center to the thickness of a 50 cent piece, tapering off toward the edges.

They are firm and tight so that the patient is unable to close her hands. Since August 20 the patient has received, as experimental therapy, four subcutaneous injections of alum-precipitated diphtheria toxoid, 0.5 cc. each. There was a local reaction for three days following the first two injections but no fever. The response has been good. Resolution of the lesions began within a week after the first injection and has been progressive. The patient is now able to close her hands with ease.

At present the lesions are purplish red, level with the surrounding cutaneous surfaces and smooth. Palpation reveals moderate infiltration. Diascopic pressure obliterates entirely the purplish hue, revealing an even, yellowish white stain.

The results of routine laboratory examinations were negative. An intradermal injection in a dilution of 1:5,000 of old tuberculin elicited a negative response. Roentgenograms of the long bones and hands did not disclose any abnormality of the osseous or articular structures. The fundi were normal.

A histologic section examined by Dr. Charles F. Sims was diagnosed as sarcoid, with the following description: The section showed a thin epidermis which was practically normal. It was covered with a nonparakeratotic scale. There was basophilic degeneration affecting many of the collagen fibers. Throughout the upper part of the corium and to the extent of the depth of the shallow biopsy specimen were numerous islands of cellular exudate. It consisted of pale-staining cells and giant cells. The giant cells had the appearance of foreign body cells rather than those of the Langerhans type. Under high power, the individual cells showed some degeneration. Occasionally plasma cells were also seen.

DISCUSSION

DR. GEORGE M. MACKEE: The diagnosis is difficult, if not impossible. The histologic picture is suggestive of sarcoid, but it is not definite. Clinically the lesion might well be sarcoid.

DR. FRED WISE: One thing in favor of sarcoid is the positive anergy to 1 to 5,000 dilution of tuberculin Koch. This is the type of eruption which the foreign authors call lupus pernio, and I believe the histologic changes in lupus pernio and sarcoid of Boeck are often similar, if not identical.

R. H. RULISON, M.D., *President*

A. BENSON CANNON, M.D., *Secretary*

Nov. 24, 1942

Sporotrichosis. Presented by DR. FRED WISE.

H. G., an American schoolboy aged 10 years, presented for Dr. Bart M. James, Newark, N. J., was first seen on Oct. 20, 1942, with an ulcerated area on the nose which was the size of a quarter-dollar and had an elevated, granulomatous border. There was also an ulcerated area of the same size on the right forearm. There was no neighboring adenopathy. This eruption had been present for approximately one month. The mother stated that there were several other children in the same school with a similar eruption. The boy had been visiting at a farm during the summer.

Direct smears of material from the lesions exhibited hyphae and spores. Aerobic cultures produced a growth on the fifth day. Anaerobic cultures were negative. Smears from the cultures showed clusters of spores and filaments. The appearance of the cultures and mounts resembled Sporotrichum schenckii.

A biopsy showed the greater part of the cutis to be occupied by an intense cellular reaction. In the upper part, the marginal portion was made up of plasma cells and some dilated blood vessels. The lower part had, besides round cells, plasma cells and a considerable increase in fibroblasts. The central part showed granular necrosis, the margin of which had numerous giant cells isolated and grouped, among which were some histiocytes. Some eosinophils were seen scattered throughout the inflammatory zone.

The Wassermann reaction of the blood was negative.

Treatment has consisted of application to the involved areas of roentgen rays, wet dressings of physiologic solution of sodium chloride and 5 per cent sulfathiazole ointment. At present he is taking 20 grains (1.3 Gm.) of potassium iodide three times a day, which is as much as he has been able to take without untoward symptoms. There has been considerable improvement.

Sporotrichosis in a 10 year old boy.

DISCUSSION

DR. FRANK C. COMBES: This is an interesting case from several standpoints. In the first place, the lesions do not follow the usual textbook picture of linear metastatic lesions. In the second place, the mere occurrence of a case of sporotrichosis is unusual, particularly in a group such as Dr. Wise and Dr. James have described. I recall having encountered only 1 case of sporotrichosis, and that was one of the usual picture, with lesions on the hands and linear metastatic lesions on the arm. I did not hear whether the presenters were able to demonstrate the organism on staining of a direct smear. This is usually impossible.

DR. BART M. JAMES (by invitation), Newark, N. J.: I understand from the laboratory that fungi were found on direct smears, which is unusual. I have not received reports from the other cases, but clinically the condition resembles sporotrichosis.

DR. GEORGE M. LEWIS: It may be that the finding of mycelium on direct smear is due to a contaminating fungus. S. schenckii is difficult to demonstrate

in the ordinary direct mounts. Cultures of the micro-organism are usually readily obtained, and this is the most reliable laboratory test for this disease. The culture is typical and confirms the clinical impression. It is of interest that several other cases have occurred in the same community. While tracing the origin of the infection may be fruitless, efforts to locate the transmitting nidus might include examination of shrubbery, such as barberry bushes and rose bushes.

DR. FRED WISE: I had the opportunity of examining this patient several weeks ago, in consultation with Dr. James. There has been a great deal of improvement under roentgen therapy combined with the internal administration of iodides.

Herpes Recurrens of the Wrist. Presented by DR. FRANK C. COMBES.

A. C., a woman aged 33, presents two groups of vesicular lesions on the flexor surface of the right wrist. These have been recurring annually each fall for the last fifteen years. She had one roentgen ray treatment six months ago to the affected area, but it did not prevent a recurrence.

I am treating this patient with vaccine virus.

DISCUSSION

DR. FRED WISE: The eruption is of interest chiefly because of its unusual location and frequent recurrences. Localized eruptions of similar character are sometimes encountered on the buttocks and thighs of women, especially during the menses.

DR. J. FRANK FRASER: I have tried the immunologic treatment with variola vaccine without satisfactory results. Inasmuch as some of the members have had success with these vaccinations, the method is worthy of further trial.

DR. GEORGE C. ANDREWS: I have just finished treating a girl who had recurrent herpes on the left thigh for about three years. I gave a series of smallpox vaccinations. The first one took, the others did not. She has been free from the eruption now for six months, which is a long time for her. Her mother is well pleased with the result. This treatment is often successful. The reason I am so enthusiastic about it is that it worked on myself. I used to have cold-sores on my lips every week or two, and I do not have them any more.

DR. PAUL E. BECHET: The site of the eruption is unusual. As far as therapy is concerned, I can report excellent results with smallpox virus in a child of 6 years who for several years had averaged from fifteen to twenty attacks of herpes facialis a year. I used the vaccine once a week for about five weeks, and in the year she remained under observation there were no recurrences.

DR. R. H. RULISON: My experience agrees with that of Dr. Fraser. I have tried this therapy a number of times with no success at all. One woman was vaccinated thirteen times, the first vaccination taking rather well while the others did not take at all. She had herpes of the lips and buccal mucosa, which was very annoying, with recurrent attacks. After thirteen vaccinations she gave up. I should like to ask about the usual interval between vaccinations. I had another patient who received six or eight vaccinations without any result. I agree with Dr. Fraser that roentgen treatment seems to quiet down the disease.

DR. FRANK C. COMBES: She does not wear any jewelry on the wrist, and besides, at one time the lesions occurred 1½ inches (3.8 cm.) higher up on the arm. I have treated a number of patients with vaccination and feel that about 60 per cent of them respond. When the lesions recur at the same site, I also give one semi-intensive dose of roentgen rays. It is therefore rather difficult to tell which one of these methods of therapy has been responsible for the cure. When the patient presented has a cold she usually has extensive facial herpes; however, this time she had the sensation of a herpes lesion, but only one small vesicle developed. It will be difficult in this case to determine the results of treatment, because the attacks occur only in the fall.

DR. R. H. RULISON: Does the patient's age make any difference in this therapy?

DR. GEORGE C. ANDREWS: I have always performed the vaccination once a week and had success in an average of 6 out of 10 cases, as Dr. Combes said. In some of the cases roentgen rays are used in addition. I have a distinct feeling that the vaccination is of real value. The child I mentioned was sent to me after she had received so much radiation locally that she had some atrophy. There was an area of atrophy on the thigh, but she still had herpes outside the atrophic area. It is peculiar that the same results are not obtained with the same method of treatment. I never had any success, for example, in the treatment of herpes zoster with solution of posterior pituitary U. S. P., although others get good results.

Eczematoid Dermatitis. Presented by DR. FRED WISE.

N. G., a man aged 35, is presented with an eruption on the trunk and extremities of three months' duration. He is employed in the department of markets, removing garbage and cleaning sewer outlets. The question has arisen as to whether the eruption is occupational in character.

The first signs of the eruption appeared on the cheeks and was acute, moist and exudative. Gradually it spread to the neck, trunk and extremities. Pruritus has been intense.

He presents a widespread pinkish-red dermatitis on the arms, forearms, hands, shoulders, preaxillary regions, thighs, legs and feet. It is dry, nonscaly and mildly lichenified. In addition to these diffusely affected areas, there are similar, isolated, oval, nummular plaques on the sides of the torso. Numerous scratch marks are present on the shoulders. There is no evidence of active tinea between the toes.

NOTE.—After the patient's presentation, a piece of tissue was removed for histologic examination on November 28. There was insufficient evidence in the specimen to warrant a diagnosis of contact dermatitis, although it was a possibility. The cutis was somewhat edematous; the superficial vessels were moderately dilated, and there was a sparse cellular reaction. In one half of the epidermis there was parakeratosis. Some of the epidermic cells showed a mild degree of hydrops (parenchymatous edema). The process was a low grade superficial eczematoid dermatitis.

DISCUSSION

DR. FRANK C. COMBES: This is a case which can be discussed from either side of the fence, depending on whether one favors the insurance company or the patient. I do not see why this eruption should not be considered as being due to contact, for the reason that I cannot conceive of its having a constitutional cause. Any one who wants to prove that this is a constitutional dermatitis is going to have a great deal of difficulty.

DR. PAUL E. BECHET: The entire clinical picture in this case, the principal features of which are the symmetric distribution, lack of vesiculation and sharply defined patches, all points to a toxic dermatitis due to an internal cause. I cannot conceive of a contact dermatitis presenting such symmetry and dryness and the presence of more lesions in the covered than in the uncovered parts of the body.

DR. GEORGE M. MACKEE: Of course, one cannot tell by a single inspection whether the eruption is dermatitis venenata or some other variety of eczema. The symmetry is against dermatitis venenata. In spite of the short duration, there is considerable lichenification, especially around the neck. There are also discoid lesions and severe itching, which makes one think of chronic lichenoid discoid eczematoid dermatitis. On the other hand, there are no penile lesions and the patient is not a Jew, which speaks against that diagnosis.

DR. GEORGE M. LEWIS: The lesions are symmetric and infiltrated, and there is extreme itching. While the histologic picture is not typical, I wonder if later on other sections will show the typical histologic picture of mycosis fungoides.

DR. A. BENSON CANNON: I should rule out the possibility of a dermatitis due to a drug, particularly phenolphthalein and arsenic. One cannot ignore the fact that the location and distribution of the eruption on the hands, face and neck suggest a contact dermatitis.

DR. R. H. RULISON: I am inclined to agree with Dr. Lewis. I think the patient will later probably show mycosis fungoides.

DR. FRED WISE: My impression is that the eruption is not any variety of contact dermatitis but rather a manifestation of some metabolic disturbance reflected on the skin. I do not entertain the diagnosis of early mycosis fungoides, because there is a lack of polymorphism of lesions and the duration, about three months, is too short for such extensive progress and widespread cutaneous involvement.

Dyskeratoid Bullous Dermatosis. Presented by DR. FRED WISE.

L. P., a Negress aged 54, registered at the New York Skin and Cancer Hospital on Aug. 18, 1942, presenting lesions of about one year's duration. She had two miscarriages in 1922. She has one son living and well. There was no history of previous disease of the skin, and the familial history was irrelevant. Her general health has been good.

The lesions began on the front of the neck. They then appeared, within a period of three months, in other locations in the following order: right and left cubital regions, posterior surfaces of the thighs, groins, middle and lower parts of the back and axillas. No new areas have been involved since.

The eruption appeared first as pea-sized to cherry-sized vesicles and bullae. The blisters were "like those from a burn" and were filled with a clear fluid. It takes two to three days before they rupture spontaneously, leaving sore, raw surfaces which become desiccated and scaly. On healing, residual pigmentation remains at the affected site. Suddenly new blisters appear in the same areas. They are occasionally pruritic. There are no seasonal variations. The patches have been drying up rapidly since she has been applying magnesium and zinc emulsion with 1 per cent of phenol.

The patches are symmetric, dark purplish red and well marginated and involve extensive and continuous zones of the integument. They surround the entire neck, like a high collar, extending down to the lower borders of the clavicles. They involve the lower part of the sternum down to and including the inframammary regions, the upper half and sides of the abdomen and the groins. On the back they extend from the middorsal region down to the perirectal area and end at the middle of the flexor surfaces of the thighs. In the cubital and left popliteal areas, dark, purplish, hyperpigmented patches are present. Located within the large pigmented bands are many ruptured vesicles and bullae oozing a somewhat cloudy and sticky fluid. There are many fresh denuded areas. Some areas are covered with scales and friable, yellowish, moist crusts. Many patches have healed with slightly raised, irregular scars, while others left only fine irregular dark brown pigmented spots which form fine networks with the normal-appearing integument.

The results of routine laboratory tests were negative. The vitamin C (ascorbic acid) content of the blood plasma was 0.8 mg. per hundred cubic centimeters (normal 0.7 to 1.4 mg.). Microscopic examination and culture for tinea of material from the breast, groin and axillas were negative. Patch tests with potassium iodide and potassium bromide, 20 per cent each, gave a negative result. Two grams of potassium iodide dissolved in 60 cc. of distilled water and given in four divided doses within two days did not produce any aggravation of the lesions.

A histologic section examined by Dr. Charles F. Sims was diagnosed as chronic benign pemphigus (Hailey and Hailey). He described it as follows: The epidermis was slightly irregular and presented elongated club-shaped rete pegs throughout most of the section. Fissures and lacunas were prominent in the epidermis. The cells lining the cavity of the aforementioned lacunas stained normally for the most part. A few, however, took a more intense acid stain, and their nuclei appeared hyperchromatic. There were no free cells or fibrin within the cavity fissure. The vessels of the upper part of the cutis were moderately dilated and were surrounded by a sparse cellular infiltration composed for the most part of small round cells, plasma cells and occasional wandering connective tissue cells. There was a parenchymatous as well as interstitial edema of the collagen in the upper part of the cutis.

DISCUSSION

Dr. George M. MacKee: I agree with the diagnosis clinically and histologically. I do not know of any treatment that is of real value. It is the most extensive eruption of this kind I have seen or heard of.

Dr. J. Frank Fraser: The clinical picture is so distinctive that one can make the diagnosis on clinical grounds alone. The histologic picture is consistent with the presenter's diagnosis.

Dr. George C. Andrews: Another point about this case which is interesting is the distribution of the eruption. One often hears about the histologic picture resembling that of Darier's disease, and the distribution here, symmetrically on the lower part of the back, in the gluteal areas, groins and axillas and on the sides of the neck, is typical of Darier's disease. I think it has not so frequently been pointed out that the distribution of this eruption is clinically like that of Darier's disease because the patients presented have not had eruptions as extensive as this patient has.

Dr. George M. MacKee: In the few cases I have had of this disease, there has been no familial history.

Dr. A. Benson Cannon: I have never encountered dyskeratoid pemphigus in a Negro before, nor have I seen a patient with lesions that are so widespread as this patient's.

Dr. Frank C. Combes: I agree entirely with the diagnosis, but what impressed me was that the lesions were so symmetric that they suggested flexural pellagra.

Dr. Fred Wise: The case is of interest because of a lack of a history indicating familial occurrence of the disease. The histologic changes are recognized as being characteristic, especially with respect to the splitting of the epidermal strata of cells.

A Case for Diagnosis (Cylindroma?). Presented by Dr. John C. Graham.

Miss B. H., aged 20, is a student nurse at the Methodist Hospital. She was born prematurely, at eight months, and during childhood suffered from urticaria and bronchial asthma. She has had none since puberty. She had an appendectomy at the age of 13 and removal of a cystic ovary at 19. In August 1941 the patient first noticed a small indurated spot on her upper lip on the left side. At about the same time she suffered for six weeks with Ménière's syndrome. The dizziness cleared up, and she only occasionally has a slight attack. The skin over the indurated area on the lip was red only at menstruation, and the induration seemed to increase in size during the menses.

She was first seen by me last spring, and since that time the area of induration has gradually increased. The area is now 2 by 3 cm. in size and is constantly erythematous. The induration is cardboard-like with sharp edges involving both skin and subcutaneous tissue and when first seen was thought to be an early morphea.

A biopsy did not confirm the tentative diagnosis of morphea, but the pathologist was unable to make a diagnosis. He suggested the possibility of cylindroma. Blood counts and the results of chemical studies of the blood were normal. The Wassermann reaction of the blood was negative. Roentgenograms of the chest were normal.

The sections showed the epidermis and corium for a depth of several millimeters. The epidermis was thin and normal except for slight hyperkeratosis on the surface and absence of the rete pegs. The corium showed collagenous or hyaline swelling. The corium was infiltrated with groups and columns of epithelial cells. The groups of cells varied in size and shape, and some of the columns anastomosed. None of the groups had lumens. The histologic picture was bizarre. The epithelial cells and their nuclei varied considerably in size and shape. The cells were oval, polyhedral or spindle shaped. The nuclei were of all sizes and shapes, and most of them were intensely hyperchromatic while a few took a lighter stain and had a dusty appearance. Two small sebaceous glands and several fine hair shafts were noted, and the tumor cells appeared to be connected with the pilosebaceous system in these areas.

DISCUSSION

DR. J. FRANK FRASER: I do not think it is possible to make a diagnosis from the clinical picture. It might be one of several diseases as far as the gross appearance of the lesion is concerned, for instance, sarcoid. There is a suggestion in the histologic picture of cylindroma. In this connection, the question comes up as to what a cylindroma is. In many cases one can differentiate cylindroma in the adenoid type of basal cell epithelioma. Poppe of Denmark defines cylindroma as composed of basal cells showing cylinders which contain mucin (Poppe, E.: Carcinoma Cutis, *Am. J. Cancer* **36**:179-192 [June] 1939). Other pathologists claim that this material is not mucin. I am not prepared to say what it is. Cylindromas are frequently seen in tumors of the salivary glands. This lesion has no connection with the mucosa. The histologic picture suggests an epithelial tumor arising from one of the glandular appendages of the skin.

DR. GEORGE M. MACKEE: Histologically, cylindroma is indicated, although I thought that some of the cells seemed to spring from the hair follicles. This patient's lesion may possibly be a basal cell epithelioma derived from appendages and giving the histologic architecture of cylindroma or trichoepithelioma, as one encounters occasionally in the morphea-like epithelioma. Clinically, the lesion is not particularly suggestive of morphea-like epithelioma. One is justified in trying one large dose of roentgen rays. If not successful, a plastic operation will be necessary.

DR. GEORGE C. ANDREWS: I am in agreement with the views of Dr. MacKee in this case, and I am rather pessimistic about the outlook for therapy. I do not think it likely that roentgen rays or radium will cure this lesion. They may exert some temporary beneficial action, but I believe some surgical treatment will ultimately be resorted to. I think the probability of local recurrence is definite. Whether it would in addition spread to other portions of the body, I do not know.

DR. FRED WISE: I believe that the diagnosis of cylindroma will prove to be correct on further histologic investigation. My personal experience with a typical cylindroma is limited to a single instance, in which the lesion occurred on the temporal region of a middle-aged woman. The tumor had attained the size of a large walnut and was completely eradicated by moderate dosages of roentgen rays, administered at monthly intervals. A broad area of induration, extending for ½ inch (1.3 cm.) or more beyond the visible margins of the tumor mass, was noted in my patient. A similar zone of induration may be noted in the patient presented by Dr. Graham. On the basis of my experience, I suggest that roentgen therapy be the method of choice for this patient. Surgical intervention should be the last resort, and one should bear in mind the resultant cosmetic defect which is bound to occur, regardless of the surgeon's skill.

DR. JACK WOLF (by invitation): The patient mentioned by Dr. Wise received 2,400 r. She had another smaller lesion located symmetrically on the other side which was excised and has remained well. The larger lesion had been present a great many years and had been removed surgically on two or three occasions, but it recurs almost immediately.

DR. GEORGE C. ANDREWS: I have seen adenomatous types of basal cell epitheliomas respond to irradiation. I do not think this lesion will respond as well.

DR. GEORGE M. LEWIS: I should favor the implantation of radium seeds or the use of radium emanation, because this modality is sometimes effective in epithelioma when roentgen rays have failed.

DR. GEORGE M. MACKEE: Concerning the patient mentioned by Dr. Wise, if I recall the histologic picture correctly, the lesion was a cylindroma as far as the histologic architecture was concerned but the cells were of the basal cell type and were embryonic. I think that is the reason it responded so well to roentgen treatment. If I remember correctly the patient mentioned by Dr. Lewis, interstitial radon emanation was used, which is more effective than distant irradiation.

A Case for Diagnosis (Dermatitis Medicamentosa [Phenolphthalein]? Parapsoriasis?). Presented by DR. A. BENSON CANNON.

M. G., a man aged 33, married, a factory worker, presented an eruption of six years' duration located in the bathing trunk area of the groins, buttocks and upper parts of the thighs, in both axillas, on the medial sides of both arms and on the contiguous wall of the chest. The patient worked in a felt hat factory as a finisher for fifteen years up to the past year. He was well up to the onset of the present eruption, which began as a "red spot" in the left groin and since then has spread gradually. There are no subjective symptoms unless the area becomes dry and slightly scaly, and then it is a little itchy and feels a little brittle. He has used ointments to keep the area soft. About five years ago the same type of lesion appeared on the arms, spreading gradually. Two years ago similar lesions appeared on the backs of both knees, but these have disappeared. The patient has been treated by physicians with local medication without any change in the eruption. He states also that he has had six or seven roentgen treatments without benefit. He has used magnesia magma, liquid petrolatum and ex-lax tablets only occasionally for constipation.

Examination shows sharply demarcated, moderately pigmented, roughened and scaly, reddish tan confluent lesions. The surfaces are striated on stretching. The scaling is only moderate. Brownish pigmentation is present particularly at the periphery of the lesions with a purplish and cyanotic appearance mottled over the lesion. Telangiectasia is present.

Examination for tinea gave negative results. The Wassermann reaction of the blood was negative. A hemogram showed 4,800,000 erythrocytes, 98 per cent hemoglobin and 8,600 leukocytes, with a differential count of 60 per cent polymorphonuclear neutrophils, 38 per cent lymphocytes, 1 per cent monocytes and 1 per cent eosinophils. The urine was normal. The histologic diagnosis was dermatitis.

DISCUSSION

DR. FRANK C. COMBES: I favor the diagnosis of parapsoriasis rather than of phenolphthalein eruption. The eruption has the variegated color which is present in both diseases. I have seen patients with parapsoriasis with lesions in exactly these locations and with exactly this appearance.

DR. PAUL E. BECHET: The diagnosis is difficult. However, I should be in favor of the diagnosis of parapsoriasis of the en plaques type because of the extensiveness of the patches, their striated, pseudoatrophic appearance and the scaling.

DR. JOHN C. GRAHAM: I had the opposite impression from that expressed by Dr. Bechet. I thought this patient had a phenolphthalein eruption clinically, and, as far as I understood the histologic picture, this diagnosis was borne out.

DR. GEORGE M. MACKEE: I favor the diagnosis of phenolphthalein eruption until it is disproved. I grant that the eruption looks like parapsoriasis, but it was stated in the history that some of the lesions have disappeared permanently. The histologic picture is in favor of something more inflammatory than parapsoriasis. There is no definite evidence of poikiloderma or of mycosis fungoides.

DR. J. FRANK FRASER: I agree with Dr. MacKee that this patient more likely has a drug eruption than parapsoriasis. There is too much cellular exudate in the microscopic picture to be consistent with the diagnosis of parapsoriasis. The histopathologic picture is consistent with a phenolphthalein eruption.

DR. FRED WISE: I favor the diagnosis of parapsoriasis en plaques. In eruptions due to phenolphthalein, exacerbation of lesions usually occurs within a few minutes or hours after ingestion of the drug. The possibility that the present eruption may later develop into a form of poikiloderma vasculare should be taken under consideration.

DR. GEORGE C. ANDREWS: I am in agreement with Dr. Wise's view in this case. It is, I think, more likely a case of parapsoriasis. The patient says he rarely took ex-lax, perhaps six times at the most. He says he seldom took any laxatives because he is opposed to them.

DR. JEROME K. FISHER (by invitation): This man told me today that he was checking up with the manufacturer for whom he worked as a hatter. It was very hot where he worked and he wore only trunks. He was a finisher of hats. He found out that they used various phenol preparations in the dyes for the felt. These lesions started just where he wore his trunks. He says that since he left this work two years ago, use of these phenol preparations has been discontinued in the manufacture and finishing of hats.

DR. A. BENSON CANNON: The patient has been under observation only a few days, and we have not had time to make a phenolphthalein test. This man said that he had made it a practice to take a cathartic containing this drug once a week or every two weeks for the last two years and that his last dose was two days before he visited the clinic. He had also taken either cascara or magnesia magma once or twice a week.

NOTE.—On Dec. 22, 1942, 2 grains (0.13 Gm.) of phenolphthalein was given to the patient, and within twenty-four hours there was a flare-up in all the lesions, with redness, swelling and itching.

Mycosis Fungoides. Presented by DR. PAUL E. BECHET.

M. S., a man aged 57, registered at the New York Skin and Cancer Hospital on June 25, 1942, presenting cutaneous lesions of ten years' duration. He does not give any history of previous diseases of the skin. For the past two or three months the patient has been having a dull pain in the right nipple area which lasts from ten to thirty minutes. The pain is relieved by eating. His health has otherwise been good.

The eruption appeared first on both malar regions and the right eyebrow as finger nail–sized, somewhat itchy spots. Three months later similar lesions developed on the left shoulder. He was treated in 1932 with twelve superficial weekly roentgen ray exposures at Bellevue Hospital, after which the lesions disappeared completely. He also received at about the same time fourteen injections of a gold compound and other injections. Two years later the patches reappeared in the same areas. He was treated with more roentgen ray exposures, after which the lesions again underwent regression. In 1937 the lesions appeared on the face and the left shoulder. He then received another course of roentgen ray exposures, and the lesions cleared up. The right shoulder and eyebrow were treated in 1939 for nine months with grenz rays (?). Two years ago the lesions reappeared on the right shoulder, the upper part of the right arm, the chest and other parts of the body.

The lesions consist of reddish brown to dark purplish red, dry, scaly and exudative plaques and fungating growths. They are generalized but are more profuse on the face, the back of the neck from ear to ear, the upper limbs and the

thighs. The abdomen, the dorsal region of the back and the legs are almost entirely free of lesions. They vary in size from 9 to 25 cm. and are well defined, moderately infiltrated and raised from 1 to 2 mm. They are round, oval, arcuate, irregular and broken, with rounded and flattened surfaces. Most of the plaques are solid throughout, while some show a clearing in the center. Others have undergone almost complete involution with only a part of the original irregular border remaining. The areas that have undergone regression are marked only by light brown pigmentation, with no atrophy. The dry patches are covered with fairly large grayish white scales, loosened at the edges but firmly attached at the centers. Diascopic pressure does not cause the slightest fading of the patches. In both axillas are pea-sized to cherry-sized nodes.

The urine was normal. The Wassermann reaction was negative, and the Kahn precipitation test gave a plus-minus reaction. The total cholesterol content, the cholesterol esters and the ratio of the esters to the total cholesterol were within normal limits. The fibrinogen in the blood plasma was 0.18 per cent (normal, 0.2 to 0.3 per cent). The sedimentation rate was 14 mm. per hour (normal male, 10 mm., Westergren method). Vitamin C in the blood plasma amounted to 0.2 mg. per hundred cubic centimeters (normal, 0.7 to 1.4 mg.). Studies of urinary androgen showed 7.9 mg. of 17-ketosteroids in a twenty-four hour specimen of urine of 1,190 cc. A hemogram done on June 27 showed a moderate leukopenia, with 3,700 leukocytes, and a normal differential count. On July 2 there was a relative polymorphonuclear leukocytosis, with a shift to the left and a high band form count, of 22 per cent. The hemogram on July 10 revealed a persistent leukopenia, 4,950 leukocytes with a shift to the left, a high volume index, of 1.33 (normal, 1.0) and a progressive reduction in the erythrocyte count (4,320,000 as compared with 5,130,000 on June 27 and 4,730,000 on July 2). The results of clot retraction and fragility tests were normal. On August 20 the hemogram was normal except for the leukocyte count of 5,400 and 13 per cent band forms.

The Mantoux test elicited a 3 plus reaction in a concentration of 1 : 5,000, while the Moro patch test gave a negative response. The sternal puncture performed by Dr. Georges Leclerc showed a normal cell count. The gallbladder was normal. The electroencephalogram did not reveal any abnormal electrocortical activity.

A histologic section examined by Dr. Charles F. Sims showed the structure of mycosis fungoides. The interpretation was as follows: The epidermis was moderately irregularly acanthotic. In parts of the section there was a crust present, and in other parts there was parakeratosis. In the upper part of the cutis and to a lesser extent in the midcutis there was a focal and diffuse moderate cellular infiltration which was polymorphous and composed of cells which varied in size and shape, as regards both their nuclei and their cytoplasms. Some of the cells were decidedly hyperchromatic, others being pale staining with one or two nuclei. The infiltration appeared to be present within the meshes of the reticulum. In the upper part of the cutis one also noted scattered chromatophores. Some of the infiltration cells had invaded the epidermis.

A letter from Bellevue Hospital stated that the patient had received a considerable amount of roentgen ray and grenz ray treatments and that no further radiation therapy should be given.

DISCUSSION

Dr. George M. Lewis: Grenz rays might be given another trial in this case.

Dr. George M. MacKee: Grenz rays, because of their long wavelength, are more potent than ordinary roentgen rays, but they have little penetration and hardly seem indicated here. Sometimes patients who seem to be roentgen-ray-fast will do well with filtered roentgen rays in large doses, one lesion at a time being treated. I suggest a filter of 3 mm. of aluminum, about 120 kilovolts and 1,200 to 1,800 r.

Dr. A. Benson Cannon: I do not think one should seriously consider maximum irradiation in a case of severe mycosis fungoides in which the tumors are becoming larger and more numerous. It is imperative that the patient have treat-

ment, and roentgen therapy remains the most effective remedy available. As for radiosensitivity, I think that this depends largely on the amount of radiation given to each particular growth. As Dr. MacKee has indicated, if one gives a large enough dose unfiltered, there is no doubt that one will obtain an immediate favorable response resulting in the disappearance of all tumors. I should not be too much concerned whether the radiation caused a moderate degree of atrophy or telangiectasia, so long as the lesions disappeared. Inasmuch as some patients with mycosis fungoides respond favorably to fever therapy, one should consider its use in this case, perhaps during the course of treatment with roentgen rays.

DR. GEORGE C. ANDREWS: I also believe that larger doses of filtered roentgen rays would be desirable for this man on localized lesions, despite what he has had before. Dr. Fraser has stated many times that mycosis fungoides is primarily a disease of the skin, while Hodgkin's disease and lymphosarcoma are primarily diseases of the lymph nodes and leukemia primarily a disease of the blood. I think perhaps if one sees a patient early enough and gives the lesions a large dose of roentgen rays, there might be some hope of aborting the disease. It might be worth while trying. I have not encountered any such early cases recently.

DR. A. BENSON CANNON: It is possible that mycosis fungoides may begin as a local condition, but it has been my experience that it is a systemic disease from its inception. I sometimes see a localized eczematized patch that will remain confined to one area for many years before other lesions appear, but even in cases of such occurrences there are sometimes outbreaks of urticaria.

DR. PAUL E. BECHET: The patient is not in the least roentgen-ray-fast. He has responded most favorably to moderate amounts of roentgen rays, but because of the large number of lesions and the fact that they both recur and appear in new locations, he has received over a period of several years considerable roentgenotherapy. Yet, it seems to me that the only hope of prolonging this man's life lies in further use of the roentgen rays, despite a past history of their active use.

R. H. RULISON, M.D., *President*

A. BENSON CANNON, M.D., *Secretary*

Dec. 15, 1942

Multiple Vitamin Deficiency; Eruption Due to Petrolatum? Presented by DR. GEORGE M. LEWIS.

I. B., a woman aged 33, is presented from the New York Hospital. For three years she has suffered from progressive weakness, loss of weight, symptoms of peripheral neuritis, bleeding, purpura, diarrhea and pain in the left side of the abdomen. The neuritic pains have been partially relieved by vitamin B therapy. The bleeding has been relieved by vitamin K therapy. There has been no evidence of involvement of the central nervous system. She has had involuntary jerkings of the right leg, difficult to control in walking. The impression was multiple vitamin deficiency with involvement of the skin, the gastrointestinal tract and the nervous system. The cause was primarily one of dietary insufficiency. Anorexia nervosa was probably a factor. At present the patient is receiving massive vitamin therapy. She has gained 1.4 Kg. in ten days, is eating more and feels stronger. Her only complaint is of pain in the legs. She has been receiving daily hydrotherapy treatments with relief of pain and can now stand unsupported.

The skin shows hyperkeratotic, follicular, dirty brown papules which exhibit excessive cornification, as evidenced by the dark comedo-like appearance, diffusely scattered over the forehead, cheeks and neck. On palpation, a hard gritty feeling is experienced. A biopsy of the skin of the face showed hyperkeratinization extending into the hair follicles to such an extent that the follicles had a cystlike appear-

ance. The epithelial cells lining them appeared atrophic. The tissue was otherwise not remarkable. The cutaneous lesions have cleared slightly after massive vitamin therapy.

DISCUSSION

DR. FRED WISE: In view of Dr. Lewis' observation of the case I am inclined to agree with his diagnosis, but I suspect that the eruption on the face may have been brought on by the use of oil or grease. It resembles the so-called oil acne.

DR. J. FRANK FRASER: This may be a case of vitamin A deficiency, but more data are necessary before the diagnosis can be confirmed. The histologic picture shows only the presence of comedos, without the inflammatory reaction seen in acne vulgaris.

DR. FRANK C. COMBES: I did not see this patient, but I was always under the impression that vitamin A deficiency was associated with excessive dryness of the skin.

DR. J. REISS (by invitation): My impression of the comedo-like eruption on the face is that it is caused by applications of petrolatum.

DR. HANS J. SCHWARTZ: I have seen this patient a number of times. The whole process has cleared up a great deal since she has been on a high vitamin diet. Just now she does not show much evidence of vitamin B deficiency, but there was a definite cheilosis on admission. She also had petechiae, showing a vitamin C deficiency.

DR. A. BENSON CANNON: I agree with Dr. Wise. I should also inquire if the patient had used any remedy on her skin containing mercury, sulfur or lead that could account for the comedos.

DR. HOWARD FOX: This patient undoubtedly suffers from multiple vitamin deficiency. The eruption on the face is, however, not my conception of the tiny papules seen in vitamin A deficiency. It has the appearance of numerous comedos due to some greasy application.

DR. R. H. RULISON: Did this patient use any medicated creams containing sulfur or mercury?

DR. GEORGE M. LEWIS: There is a history of using petrolatum over a period of several months or years before the appearance of the eruption. Therefore, an eruption due to this substance naturally came to mind. There is no question that this patient has an avitaminosis. However, whether the cutaneous lesions now present are also due to the avitaminosis is, of course, open to question. The eruption has improved considerably in just a few weeks with high vitamin therapy. When Dr. Schwartz and I first saw her, the lesions were closely grouped. There was an enormous number of comedo-like papules with a nutmeg grater feel which was not quite typical for the greasy comedos that one sees in oil acne.

A Case for Diagnosis (Winter Eczema?). Presented by DR. FRED WISE.

R. M., a man aged 47, registered at the New York Skin and Cancer Hospital on Dec. 15, 1942, presenting lesions of three months' duration. His general health has been good. He gives a history of having recurrences of the same eruption for the past five years. It usually begins in October and disappears completely with the onset of the warm weather in May. The eruption usually appears first on the flexor surfaces of the wrists, and within a month it extends upward to the bends of the elbows. At the same time similar eruptions appear on the hips and in the groins. For the past few years the rash has appeared only on the aforementioned areas, while this year it has also spread on the trunk. It is slightly itchy. The patient recently applied a lotion which aggravated the eruption, imparting to it a burning sensation.

The lesions are located on the trunk and extremities, being most pronounced on the volar surfaces of the limbs and more profuse on the abdomen than on the back. The lesions are perfectly symmetric and superficial and consist of irregular, brownish red, erythematous patches, discrete and confluent, poorly defined and slightly scaly. In some areas these patches have coalesced to form large plaques.

There are numerous closely arrayed, dark brown–pigmented spots, caused by repeated exposures to the sun, on the extensor surfaces and sides of the upper extremities, the legs and the lower half of the thighs. There is a moderate diffuse alopecia of the scalp, but the scalp is otherwise unaffected.

The results of routine laboratory tests were negative. A section examined histologically by Dr. Charles F. Sims showed a "superficial exudative inflammatory process." The epidermis presented no noteworthy changes. The cutis revealed the following characteristics: There was a moderate interstitial edema throughout the upper and middle parts of the cutis. The vessels of the upper part of the cutis were dilated and surrounded by a sparse cellular infiltration composed of small round and occasional connective tissue cells.

NOTE.—Most of the lesions have since undergone involution following the application of an ointment consisting of 4 per cent salicylic acid in petrolatum.

DISCUSSION

DR. A. BENSON CANNON: I should not consider the diagnosis of seborrhea or psoriasis because the location, distribution and character of the lesions do not remind me of either disease. If one were able to rule out the possibility of a drug as the cause, I should think of some external irritant. I do not think the condition is a disease of the skin.

DR. PAUL E. BECHET: The lesions have a distinct conformation and sharply outlined borders. Of course, to my mind the patient has a secondary dermatitis, but what the primary lesions are is more difficult to determine. I thought perhaps that the scaliness was not that of psoriasis but looked as if at one time the lesions had oozed a bit and dried. This man may have parapsoriasis of a scaly type with a secondary dermatitis or even a pityriasis rosea. Between those suggestions there is so much room for error that they are not of much value.

DR. FRANK C. COMBES: I cannot see that this patient has anything but a winter dermatitis. I could not see the remotest resemblance to psoriasis. I think if he went to Florida he would not have his eruption.

DR. FRED WISE: I regard this patient's condition as a probable seborrheic dermatitis.

A Case for Diagnosis (Lupus Erythematosus?). Presented by DR. JOHN C. GRAHAM.

A. B., a man aged 52, a carpenter, was first seen three days ago. He complained of an eruption on the lower lip of two and one-half years' duration. During warm weather there have been no subjective symptoms, but in the winter there have been some cracking and burning. He has never had any other disease of the skin, and his general health has been good. For the past ten weeks he has been under the care of another dermatologist, who has been giving him weekly injections of a bismuth compound.

The patient presents a sharply demarcated violaceous lesion on the lower lip. The area extends nearly across the whole lip. The surface is smooth, and there is slight thickening. There are white punctate areas scattered throughout the involved area, but none of these is of great enough extent to be palpable. There is a moderate amount of pyorrhea, and there is a blue line on the gums from the bismuth. There are no other lesions on the body and no lesions on the penis or the mucous membranes of the oral cavity.

DISCUSSION

DR. PAUL E. BECHET: The lesion is well circumscribed. It has a rounded border, and the scales are extremely adherent. On the left side of the lip there is distinct atrophy. For these reasons, I should consider the diagnosis of lupus erythematosus as the most plausible one.

DR. FRANK C. COMBES: The vermilion border of the lip was entirely free of any eruption. I have never seen lupus erythematosus of the mucosa of the lip

without involvement of the vermilion border. This eruption strongly suggests leukoplakia. The patient is an excessive pipe smoker.

DR. J. FRANK FRASER: I cannot entertain the diagnosis of either lichen planus or leukoplakia. I favor the diagnosis of lupus erythematosus. I suggest a biopsy. If this eruption is lupus erythematosus, what changes should be present in the histologic picture? English pathologists claim that the initial lesion in this disease is a cellular exudate and that the changes in the collagenous tissues (fibroid degeneration, etc.) represent an end process, while Klemperer and his associates insist that the fundamental lesion of lupus erythematosus is in the connective tissue system. At a recent meeting of another society I showed sections which could be interpreted as lending support to both of these views. One section showed only collagenous changes, with areas of basophilic degeneration immediately under the epidermis. In another section of tissue, removed from a different lesion, the cellular reaction dominated the histologic picture. Fibroid degeneration or other collagenous changes were not observed.

DR. HOWARD FOX: In a case of scaling confined to the lip, one can make only a tentative diagnosis from its appearance. Lupus erythematosus would be a possibility. While the diagnosis could be settled by a biopsy, I understand the patient will not permit this to be done. I suggest that a leukocyte count be made.

DR. GEORGE M. LEWIS: I suggest a biopsy, as it is important to settle the diagnosis. Healing of the wound made for removal of biopsy tissue is usually prompt and seldom complicated by infection.

DR. JOHN C. GRAHAM: I suggested that it would be a good plan to have a piece removed from the lesion, but the patient refused definitely. After I become better acquainted with him I may be able to persuade him to have a biopsy done. He is a carpenter and has been exposed to the sun a great deal. That in no way increases the lesions. The eruption is made worse or more uncomfortable by cold during the winter, but in the summer, when he is exposed to the sun while working out of doors, it has not been made worse. While that does not rule out lupus erythematosus, it does open the diagnosis to question.

Extensive Dermatitis Medicamentosa (Gold Salts). Presented by DR. HOWARD FOX.

J. N., a man aged 44, a waiter, born in Luxembourg, came to the United States twenty-two years ago. He had always been in good health until August 1941, when painful swellings of the joints of both hands developed. Within two weeks "all of the joints of the body" were painful and he became temporarily bedridden. On September 22 he went to the Vanderbilt Clinic, where a diagnosis of rheumatoid arthritis with chronic tonsillitis was made. He was treated by intramuscular injections of solganol B (aurothioglucose) from Oct. 17, 1941 to Jan. 7, 1942, receiving a total of 1.06 Gm. of the gold compound. The first injection was 10 mg., followed by two injections of 25 mg. each and then by two injections of 50 mg. each. Subsequently, he received, at weekly intervals, 100 mg. at each treatment. After this he was completely relieved of arthritis, the injections being discontinued on Jan. 7, 1942. The patient then went to Florida to work.

The following information was given by Dr. A. Benson Cannon regarding laboratory procedures: The Kline reaction of the blood was negative. The erythrocyte sedimentation rate gradually fell in the course of three months, from 47 to 8 mm. in one hour. A biopsy was reported as showing probably dermatitis medicamentosa (possibly lupus erythematosus). A second biopsy of material from the left axilla was performed at the New York City Hospital and showed mild hyperkeratosis, the epidermis being otherwise atrophic. The corium, particularly the papillary layer, was edematous and moderately infiltrated by lymphocytes, chiefly about the blood vessels. There were many chromatophores, especially in the papillary body, containing many fine and coarse pigment granules. There were no wandering connective tissue cells. Extravasated red blood cells were seen rather frequently. The diagnosis was chronic atrophic dermatitis with pigmentation.

On February 26 an eruption appeared on the wrists and forearms and inner aspects of the thighs, and within two days it had spread over the greater part of the body with the exception of the face. The eruption was accompanied by itching for the first six weeks, after which time this symptom disappeared completely. There was considerable loss of hair in the temporal region and the eyelashes fell out completely. In April the eruption spread to the face, scalp and mouth, and he then returned to New York for treatment at the Vanderbilt Clinic. He was given tablets of ascorbic acid for five days without improvement. He was later referred to the New York City Hospital, where he was given injections of sodium thiosulfate three times a week, for a total of fifty injections. The patient stated that the eruption became about "20 per cent better" after this treatment.

The patient presents a generalized, symmetric, profuse eruption of the face, trunk and extremities. The ears, genitalia and soles are the only unaffected areas. The greater part of the eruption consists of yellowish brown macules varying in size from that of a pea to that of a finger nail. The lesions are smooth and are devoid of subjective symptoms. The great majority of the lesions are discrete, though in certain areas, notably the waist line, there is considerable confluence, forming a broad girdle. The appearance of the eruption suggests one due to phenolphthalein. In certain areas, especially the flexor surfaces of the forearms and the palms, there are numerous telangiectases intermingled with the brown macules. On diascopic pressure, the telangiectases disappear, but no change in color is shown by such pressure on the brown macules. In a few areas there are also whitish atrophic streaks and small macules intermingled with the brown macules and telangiectases, giving the lesions a poikiloderma-like appearance. At the commissures of the mouth are superficial triangular white lesions, suggestive of leukoplakia.

The general health appears to be excellent, and there is no evidence of arthritis.

DISCUSSION

DR. FRANK C. COMBES: I think this case is the first one that has ever been presented here of an eruption of this type following administration of a gold compound. In certain respects the eruption simulates the rain drop pigmentation due to melanin of arsenical pigmentation. The peculiar feature here is the telangiectasia and atrophy. Of course, these heavy metals are toxic to the cutaneous capillaries, and there is no reason why they should not produce poikiloderma-like eruptions. It is an unusual case. The question as to whether the condition should be called chrysiasis will come up in the discussion. I think this term should be confined to local deposits of gold, such as the bluish discoloration which occurs in cases of accidental injection of gold into the skin. I think the eruption in this case should be called dermatitis medicamentosa due to gold.

DR. PAUL E. BECHET: Dr. Fox's case is extremely interesting. Eruptions with poikiloderma-like changes are rare but have been reported after the use of heavy metals, particularly arsenic (Vuletić, A.: *Arch. f. Dermat. u. Syph.* **169**: 436 [Dec.] 1933). However, I believe that this is the first instance in which poikiloderma-like lesions have occurred after the use of gold.

DR. SIDNEY LANDY (by invitation): I should like to know if this patient has shown any constitutional disturbances.

DR. HANS J. SCHWARTZ: This is an interesting and unusual case. I agree with the diagnosis as presented.

DR. A. BENSON CANNON: I think that one not infrequently sees pigmentation and telangiectasia after a severe gold dermatitis, although not as pronounced as in the patient presented. Dr. Ralph Boots, in charge of the arthritis clinic at Columbia University, uses large doses of gold compounds intramuscularly in the treatment of rheumatic conditions. I believe that he has reported 13 per cent of cures and a fair portion of the other patients were benefited by the injections. I think that so many cases of gold dermatitis are encountered in arthritis clinics because of the large doses administered and the retention of the preparation when injected in the muscles. Not only is the skin frequently involved in gold intoxi-

cation, but also the gastrointestinal tract. Bleeding from the mucous membranes of the stomach and severe ulcerating colitis not infrequently follow. I have observed more than 1 case in which there was bleeding of the gastrointestinal tract with enlargement of the spleen and secondary anemia, symptoms suggestive of gastric or duodenal ulcer or Banti's disease. I know of 1 such case in which a splenectomy was performed. Many more cases of gold poisoning were encountered when the arthritis clinics first began to use injections of gold compounds for the treatment of rheumatic conditions than now, since the physicians have become better acquainted with the toxic effects of the drug.

DR. GEORGE M. LEWIS: I have never seen a patient showing the manifestations presented by this patient, but I accept Dr. Fox's interpretation. As to the question of reactions to gold, it is an interesting one, and little is known about the mechanism. Some patients take large quantities of a gold compound without any untoward reactions, whereas others with comparatively small doses have a severe reaction. At present there is no way of estimating the amount of gold in the blood, but a method for this would be a great help in determining whether this phenomenon is toxic or allergic.

DR. A. BENSON CANNON: A symposium was presented before the American Medical Association a few years ago on the treatment of arthritis with injections of gold compounds. There were a great many reports in the English literature on the subject, and it was largely due to these optimistic reports that the treatment was begun in America.

DR. HOWARD FOX: An extensive eruption like this one should be a lesson to specialists in arthritis who often use large amounts of gold salts and, as one of the guests just said, do not cure all of their patients. Little is said in American textbooks on dermatology about eruptions due to gold salts. Most of the eruptions I have seen have been of the eczematous type, at times, as in this patient, associated with stomatitis. I avoided using the term chrysiasis because it was not included in the recent edition of Standard Nomenclature of Disease. The term would simply mean an increase of gold salts in the tissues and not necessarily in the skin. Most of the gold, I understand, is deposited in the kidneys and liver and is excreted mainly by the kidneys.

DR. PAUL E. BECHET: Dr. Fox's remarks relative to renal insufficiency in cases like the one presented are supported by Ayres (ARCH. DERMAT. & SYPH. **23**:107 [Jan.] 1931), who stated that he uses the phenolsulfonphthalein test in order to detect renal insufficiency prior to the use of gold sodium thiosulfate, thereby saving himself from some bad results. The leukocyte count in my opinion is equally important (*New York State J. Med.* **42**:609 [April 1] 1942), and these two procedures should be repeatedly done throughout a course of gold therapy in lupus erythematosus.

DR. A. BENSON CANNON: I think that one should be on the lookout for symptoms referable to the gastrointestinal tract in all patients who are being treated with large doses of a gold compound, either intramuscularly or intravenously. I have known other cases in which there were attacks of vertigo, temporary lapses of memory, etc., while a gold compound was being administered.

Urticaria Pigmentosa (Nodular Lesions). Presented by DR. FRED WISE.

S. D., a man aged 44, referred by Dr. N. Persky, registered at the New York Skin and Cancer Hospital on Dec. 8, 1942, presenting lesions of one year's duration. The family history is irrelevant. The patient had infantile paralysis at the age of 18 months and has been in good health since. The first lesion appeared on the lumbar region. About two months later four similar spots appeared on the middle of the sternum and one spot a month later on the right side of the face. Then spots began to appear on the rest of the face, the chest, the right groin and other parts of the body in that sequence. Most of the lesions appeared between June and October. None of them have, to his knowledge, undergone

regression. They commenced as flat spots or as roundish "pimples." The flat lesions remained as such, while the raised, roundish nodules enlarged within six weeks. They were at first light red, but within a month they gradually became purplish brown. They are occasionally pruritic.

The lesions are generalized except for the palms and soles. The surfaces are smooth and nonscaly. They are numerous, fairly symmetrically distributed, closely aggregated but discrete. They consist mostly of flat, match head–sized to bean-sized macules, of a uniform dull brownish red color, distributed along the lines of cleavage of the skin, best seen on the trunk, with the long axis directed downward and forward. Many of the lesions are slightly raised, rounded and somewhat infiltrated, with purplish red centers and with a darker hue at the periphery. A few raised nodular growths are seen on the inner surfaces of the thighs. They are fairly hard and freely movable on the subcutaneous tissue. These are dark purplish and have irregular purplish black peripheral zones. There is a solitary saucer-shaped depressed spot on the right frontal region at the junction of the hair margin. All the lesions are painless, nontender and not atrophic. None, even the flat lesions, are altered noticeably on diascopic pressure. On being rubbed they become turgescent and bright red and an urticarial-like erythematous halo appears, which persists for some time. There are no palpably enlarged lymph nodes.

The results of routine laboratory tests were negative except for a leukocyte count of 10,400 and 15 per cent monocytes. The chemical examination of the blood serum showed: total proteins 8.8 per cent (normal 6 to 8), albumin 5.9 per cent (normal 4 to 5) and globulin 2.9 per cent (normal 2 to 3), which gives the normal ratio of 2. The reaction to an intracutaneous tuberculin test was normal in a concentration of 1 : 5,000.

A nodular lesion stained with hematoxylin and eosin was examined by Dr. Charles F. Sims and described as follows: The epidermis was moderately irregularly acanthotic. Beginning at the under surface of the epidermis and extending downward into the middle of the cutis was a dense cellular mass composed of the following types of cells: There were numerous connective tissue cells and capillaries lined with endothelial cells running in different directions and giving the mass a reticulated or network-like appearance. Within the meshes of this network there were numerous cells with large round or oval nuclei with one or more nucleoli and a distinct hyperchromatic nuclear network. Surrounding the nucleus was an eosinophilic granular cytoplasm with an ill defined cell wall. Throughout the mass were numerous dilated capillaries, some of which were filled with blood. Increased pigmentation was present in the lower portion of the epidermis which did not lie over the mass. The section stained with methylene blue showed the typical agglomeration of mast cells characteristic of urticaria pigmentosa.

DISCUSSION

Dr. J. Frank Fraser: The clinical picture is unusual, but the histologic picture confirms the presenter's diagnosis.

Dr. Howard Fox: Dr. Combes should be congratulated on making the correct diagnosis clinically, especially as no one else made this suggestion. The rather unusual location on the face, the absence of a yellowish brown color and the papular elevation are unusual features of urticaria pigmentosa.

Dr. Sidney Landy (by invitation): I should like to ask whether this patient is the one who was presented before the Academy of Medicine a few weeks ago with a diagnosis of mycosis fungoides, based on histologic study.

Dr. Frank C. Combes: This patient has lesions on the thighs that look less like urticaria pigmentosa than the lesions on the body. He has nodules there as big as a hazelnut. However, I agree with the diagnosis.

Dr. Fred Wise: The histologic picture is unusual with respect to the extremely large number of mast cells and their dense arrangement.

There was a general agreement with the diagnosis by all the members.

Sarcoma of Kaposi. Presented by DR. FRED WISE.

B. H., a man aged 65, was presented before the New York Dermatological Society in October 1942 (ARCH. DERMAT. & SYPH., this issue, p. 733). He is presented again for suggestions for therapy.

DISCUSSION

DR. HOWARD FOX: In my opinion, there has been definite improvement in the ulcers since the previous presentation. They are now much more superficial. If further roentgen treatment is not considered proper, the lesions could be excised or desiccated. I should not think of amputating the hand, as was suggested in an informal discussion. Because of the extent and severity of the disease, I do not think the patient will live much longer.

DR. A. BENSON CANNON: I should think one would have to wait from six to eight weeks before it could be determined whether the roentgen rays had been effective. I believe the patient's last treatment was only a week ago. I should advocate fever therapy and arsenic. I should not consider amputating the extremity at this stage.

DR. J. FRANK FRASER: I agree with Dr. Fox that the ulcers show improvement since the previous presentation. The appearance of some of the lesions suggests angioma. Cases have been reported in which necropsy has revealed a generalized angiomatosis (Lang, J. F., and Haflhofer, L.: Ueber die Auffassung der Kaposischen Krankheit als systematisierte Angiomatosis, *Ztschr. f. Krebsforsch.* **42**:68, 1935). Kaposi in his original article reported a histopathologic picture of round cell sarcoma. The condition recognized as Kaposi's disease today does not show a microscopic picture of round cell sarcoma. I observed a patient with lesions similar to those in Dr. Wise's case; there was a spread to distant organs, and the patient died within a year. Permission for a necropsy was not obtained, and it was not determined whether the spread was of multiple primary origin or due to metastasis from the cutaneous lesions. Cavernous angiomas rarely metastasize to the lungs (Boyd, W.: The Pathology of Internal Diseases, ed. 3, Philadelphia, Lea & Febiger, 1938, p. 316).

DR. PAUL E. BECHET: I do not believe any amount of roentgen therapy will change the eventual fatal termination in this case.

DR. HOWARD FOX: Would Dr. Cannon give fever therapy to a person of the patient's age and in such poor condition?

DR. A. BENSON CANNON: Yes, I think fever therapy should be used. The patient appears well to me, and I do not share the pessimistic opinion regarding the outcome voiced by most of the other speakers. I have seen several patients with extensive lesions of Kaposi's sarcoma who have lived for many years.

DR. FRED WISE: I am glad to hear that several members regard the ulcers as having improved. I suppose I do not notice the difference because I see the patient so frequently. He has received large doses of an arsenic compound by injection previously and is now taking arsenic pills (asiatic pills). I thought of excision of the ulcers followed by full thickness skin grafts, as a palliative treatment only, of course. The man is discouraged.

Lupus Erythematosus (Discoid Type); Macular Atrophy (Primary). Presented by DR. GEORGE M. LEWIS.

C. W., a married woman aged 32, is presented from the New York Hospital. Some atrophic lesions on the body were noticed first eleven years ago, gradually increasing in number since then. None of the lesions has been inflamed at any time. The lesions of lupus erythematosus appeared first nine years ago and have persisted in spite of considerable therapy in another institution. The atrophic lesions are present on the back and buttocks and range in size from that of a split pea to that of a coin. There is some ballooning of a few larger lesions. A tendency to follow the lines of cleavage is noted. The largest lesion of lupus

erythematosus is on the right cheek, where there is a plaque about 2½ inches (5.3 cm.) in diameter. Smaller similar lesions are present on the left ear and on the scalp. The Wassermann reaction of the blood was negative. The urine and a blood count were normal. The sinuses did not show any evidence of infection. There was roentgenologic evidence of pulmonary emphysema and bilateral basilar pleural thickening. The patient also has a cystocele and a rectocele.

DISCUSSION

DR. FRANK C. COMBES: This type of case has been previously reported and is interesting. It brings up the possibility that so-called idiopathic macular atrophy may be based on some systemic intoxication. I have a case in which the condition, now extensive, followed a streptococcic tonsillitis ten years ago.

DR. PAUL E. BECHET: Here is a typical example of two separate and distinct dermatoses occurring in the same patient, a coincidence much more frequent than is indicated in the literature. I have always thought that the apparent abhorrence of the average dermatologist to make two diagnoses in the same case when clearly apparent was more or less of a phobia, as in a long clinical experience two distinct dermatologic entities occurring in the same patient have not infrequently come under my observation.

DR. SIDNEY LANDY (by invitation): There is at present in Bellevue Hospital a patient with two similar eruptions, a woman of about the same age as this patient. There is bilateral atrophy of the face, which I thought was due to lupus erythematosus, and at the same time there is macular atrophy on the body.

DR. HOWARD FOX: I agree that the patient presents two separate clinical entities. As the cause of both is unknown, it is conceivable that they might have the same causation.

Pemphigus Vulgaris (Cured?). Presented by DR. A. BENSON CANNON.

I. Z., a man aged 55, was admitted to Vanderbilt Clinic on Sept. 23, 1942, to be treated for multiple bullous lesions of the skin and mucous membranes. The onset of the eruption was in May 1940, with bullae on the scalp, face and neck. The patient was treated at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital with salves and lotions. The bullae spread to the skin of the body and extremities in March 1941, accompanied by constitutional symptoms of weakness, fever (temperature of 103 F.), loss of 15 pounds (6.8 Kg.) in weight, insomnia and pain in the cutaneous lesions. He was admitted to Fordham Hospital in April 1942, where he remained nineteen weeks. The fever disappeared with antiseptic baths and local applications, but the bullae continued to spread and the patient became weaker. The diagnosis of pemphigus was made and a bad prognosis given to the family.

I saw the patient in consultation and advised sponging the body with potassium permanganate solution and dressing all of the lesions with an ointment containing 5 per cent ichthammol and 1 per cent phenol in petrolatum, forced fluids, alkalis, a high caloric diet and vitamin therapy. Six weeks of this treatment was followed by weekly injections of arsphenamine, and the patient's general condition greatly improved, as did the cutaneous lesions. Only occasional bullae reappeared, and the patient was able to go home on September 1. Treatment was carried on at home until September 23, when he was admitted to Vanderbilt Clinic.

At Vanderbilt Clinic the patient has had estrogenic therapy, 50,000 units three times a week; vitamin D therapy, 450,000 U. S. P. units three times a week; sodium citrate, 15 grains (1 Gm.) twice a day; sodium bicarbonate, 1 teaspoon three times a day; a vegetable diet, and forced fluids. Improvement has been steady and continuous. All lesions have disappeared, and no new lesions have appeared in the last three and one-half weeks. Vitamin therapy is being continued.

The Kline and Wassermann reactions of the blood were negative. Urinalysis showed an acid reaction, a 2 plus reaction for albumin, no sugar, a few leukocytes

and a few fine granular casts on microscopic examination. The blood count showed 3,580,000 erythrocytes and 7,800 leukocytes, with a differential count of 56 per cent polymorphonuclear leukocytes and 44 per cent lymphocytes. There was 72 per cent hemoglobin.

DISCUSSION

DR. FRED WISE: I congratulate Dr. Cannon on this excellent response to his therapy.

DR. R. H. RULISON: Of course pemphigus does show remissions, but this patient shows a striking improvement.

DR. HOWARD FOX: This is a most gratifying remission for pemphigus. Did Dr. Cannon ascribe this to the administration of arsphenamine?

DR. A. BENSON CANNON: The patient was given eight injections of arsphenamine.

DR. FRANK C. COMBES: What estrogenic substance did Dr. Cannon use?

DR. A. BENSON CANNON: The preparation was estrone (theelin). The patient had six weeks of alkalis, high vitamin diet and injections of crude liver extract followed by six weekly injections of old arsphenamine. He improved so much that he was able to be discharged from the hospital and reported to the Vanderbilt Clinic, where his treatment was continued with estrogenic substances given by hypodermic injection and later by mouth and large doses of vitamin D. The medicine was very expensive, being about $54 for the treatment of 1 patient for two months. This high cost was reduced by getting the drugs put up in tablet and capsule form so that they could be taken by mouth.

Tuberculosis of the Hypoderm. Presented by DR. FRANK C. COMBES.

G. M., a British Indian aged 23, a seaman, had never had any cutaneous disease prior to four months ago. At that time several deeply situated lumps appeared on his left forearm near the elbow.

At present the patient shows four nodules. The largest is painless, is located in the hypoderm and measures about 2 cm. in diameter. It is located anterior and slightly proximal to the left medial epicondyle. It is freely movable and is not attached to the overlying skin. From both the superior and inferior poles of this nodule, hard, nontender, cordlike bands extend for several centimeters up and down the inner aspect of the arm and forearm, following the course of the regional lymphatics. The axillary nodes are not enlarged.

A second nodule having similar characteristics is situated on the dorsal aspect of the left arm about 5 cm. proximal to the elbow. This is attached to the overlying skin and has a small opening exuding a thin purulent fluid. Two more small nodules are present on the back of the forearm. Hard cordlike bands connect these nodules with each other.

The blood and urine were normal. Roentgenologic examination of the chest showed a residual bronchiectasis. Histologic examination of one of the lesions showed granulomatous infiltration of the subcutaneous tissue with caseation tuberculosis. Several acid-fast stains were made, but only one tubercle bacillus was seen. Other stains failed to show parasites.

Eczematoid Dermatitis. Presented by DR. FRED WISE.

N. G., a man aged 35, was presented on Nov. 24, 1942 (ARCH. DERMAT. & SYPH.). Histologic examination showed the picture of an ordinary eczema. I have learned nothing further about the case.

A Case for Diagnosis (Cylindroma?). Presented by DR. JOHN C. GRAHAM.

B. H., a woman aged 20, was presented on Nov. 24, 1942 (ARCH. DERMAT. & SYPH., this issue, p. 747). She was treated with radium therapy. Four days after treatment the lesion was only half its original size, and now, after about two weeks, it is completely gone. There is not the slightest bit of induration present at this time.

Book Reviews

Familial Nonreaginic Food-Allergy. By Arthur F. Coca, M.D. Price, $3.00. Pp. 160. Springfield, Ill.: Charles C Thomas, Publisher, 1943.

In this little volume, the author describes his method of approach to the diagnosis and treatment of certain "allergic" diseases which he has grouped into a special category and for which he has coined the term "familial nonreaginic food allergy." This group includes urticaria, migraine, gastrointestinal allergy, neuralgias and a "number of more or less serious conditions hitherto unrecognized as allergic."

Throughout the book, the author stresses the importance of food in the production of symptoms. Other causative agents include drugs, metals (from cooking utensils), fumes and dusts.

Two outstanding features of his newly recognized category of allergic diseases are: (1) absence of atopic reagins and therefore negative reactions to cutaneous tests and (2) acceleration of the pulse rate during the manifestation of allergic reactions.

By means of trial diets and determinations of the pulse rate, the author was able to identify causative foods in a number of diverse syndromes and symptoms, including headache, mucous colitis, dizziness, migraine, neuralgia, nervousness, abdominal pain, physical tiredness, canker sores, intestinal bleeding, nausea, vomiting, angina pectoris, heartburn, extrasystoles, psychic depression, constipation, conjunctivitis, pain in the chest, diarrhea, emotional instability, petit mal, pain in gallbladder, chronic rhinitis, angioneurotic edema, allergic sore throat, epistaxis, chronic cough, acne and bronchial asthma. The avoidance of incriminating foods resulted in the disappearance of symptoms and specific tachycardia.

A number of charts, tables and cases are presented to prove the author's contention. However, the evidence as a whole is meager and the number of patients with most of the diseases and syndromes treated are too few to permit one to draw definite conclusions.

The book makes interesting reading, but the author should be prepared for a good deal of skeptical comment.

A bibliography of about ninety-five references is scattered throughout the text.

There is a misprint in the middle of page 58; the word "lamp" should be "lamb."

CORRECTIONS

In the article by Dr. Evan W. Thomas and Dr. Gertrude Wexler entitled "Rapid Treatment of Early Syphilis: Report of Two Hundred and Eighty Treatment Courses with Mapharsen Alone and Five Hundred and Forty-Nine Treatment Courses with Mapharsen Combined with Fever" (ARCH. DERMAT. & SYPH. **47**:553 [April] 1943), in the first item in Plan 1 on page 555, the word "Two" should read "One."

In the list of specialists certified by the American Board of Dermatology and Syphilology in the February issue (ARCH. DERMAT. & SYPH. **47**:253, 1943) the titles of Dr. Isadore Botvinick and Dr. Joseph Markel were inadvertently omitted. Both are passed assistant surgeons in the United States Public Health Service at Bethesda, Maryland.

In the article by Drs. George M. MacKee, Arthur Mutscheller and Anthony C. Cipollaro entitled "Time Factor in Irradiation," in the April issue (ARCH. DERMAT. & SYPH. **47**:490, 1943), the word "casual" in the first line of the third paragraph under "Summary and Conclusions," on page 497, should read "causal."